Altitud Illn ss

Travelers are drawn to high altitude places in ever increasing number- Nepal alone now receives more than one hundred thousand trekkers from around the world every year. It can be easy to under-estimate the dangers of altitude illness; deaths from these conditions are all the more tragic because they are entirely preventable.

Mountain climbers, serious trekkers, romantics sauntering through the foothills of the Himalayas, native porters, skiers in North America and Europe, pilgrims to high altitude shrines, diplomats posted to La Paz or Lhasa, miners in South America, and Everest marathon runners have something in common: they are all exposed to the effects of high altitude, and may be at risk from a potentially fatal but eminently preventable problem: Acute Mountain Sickness, commonly referred to just as AMS.

AMS consists of headache plus any one of the following symptoms in different degrees: nausea tiredness, sleeplessness or dizziness, occurring at altitudes of around 8000 ft or higher where pathophysiological changes due to lack of oxygen may manifest. Another term, "altitude illness', is also widely used - an umbrella term that includes the benign acute mountain sickness and its two life-threatening complications, water accumulation in the brain (high altitude cerebral edema, HACE) or high altitude pulmonary edema (HAPE, water accumulation in the lungs). The latter two complications may follow AMS, especially when people continue to ascend in the face of increasing symptoms. In keeping with the Jesuit tradition of painstaking documentation, Father Joseph de Acosta, a sixteenth century Spanish Jesuit priest, is credited with having first described the effects of high altitude in humans. In vernacular Nepali, mountain sickness is called "lake lagne": in Sanskrit it is aptly called "damgiri" ("dam" means breathlessness and "giri" means mountain).

Those most at danger from complications are people who do not "listen to their body", and heed the early warning signals of AMS; they can go on to suffer from HAPE and HACE and may even die-a process that has been carefully documented in important autopsy studies performed by Walter Bond and John Dickinson during the Seventies in the old Shanta Bhawan hospital in Nepal.

Chronic mountain sickness is an entirely different condition, recognized by Carlos Monge Medrano in high altitude long-term residents of South America during the Twenties. Such maladaptation is seldom found in the Sherpas or Tibetans, possibly due to thousands of years of exposure to high altitude living. (south Americans populations are relative newcomers to high altitude.) The present discussion will be confined to acute exposure to altitude in short-term sojourners.

Mountain climbers, serious trekkers, romantics sauntering through the foothills of the Himalayas, native porters, skiers in North America and Europe, pilgrims to high altitude

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[Top]

Acute Mountain Sickness

If a participant on an Everest trek suffers from a mild headache and nausea at Namche Bazaar (12,300ft), he might take an aspirin and wait for these symptoms to go away; however if the symptoms progress to vomiting and a splitting headache, he must assume that he is suffering from AMS and make plans to descend. It is amazing how many people in this situation ignore the dangers and continue to ascend with their friends, trying to blame their symptoms on poor fitness or flu. For some people, it's the high investment of time, effort and money, for others perhaps it's peer pressure or reluctance to accept defeat. A further is that many in the burgeoning adventure travel industry are clueless about mountain sickness.

AMS may set in within hours to days of arrival at high altitude: the onset of symptoms is usually gradual, which is why it is so vital to watch out for early warnings: does a person feel excessively tired; is she the last one to drag herself in to camp?

What causes AMS?

AMS is caused by a lack of oxygen. Although the proportion of oxygen in the atmosphere always remains the same (21%), as we go higher the "driving pressure" decreases. The driving pressure depends directly on the barometric pressure, and forces oxygen from the atmosphere into the capillaries of the lungs. Reduced driving pressure results in decreased saturation of oxygen in the blood and throughout the tissues.

Just what causes some people to suffer from AMS but not others is largely unknown, but there are clear-cut and important preventive factors that are now well- established (see below). The exact mechanism (pathophysiology) of AMS has similarities to that of HACE.

[Top]

High Altitude Cerebral Edema (HACE)

Our trekker in the above example would probably go on to suffer form HACE if he continue to ascend despite the headache and vomiting; the symptoms of HACE are an extension of those to AMS.

From fatigue, there is progression to lethargy and then to coma. Or there may be confusion and disorientation, A useful test is to see if the person can walk a straight line. If he walks like a drunk or is unsteady, it has to be assumed that he has life-threatening HACE and needs to descend promptly with assistance. This situation is serious enough to justify immediate helicopter evacuation.

HACE is probably caused by shifts of fluid into the tissues of the brain. Reduced oxygen levels cause swelling within the confines of the bony skull. The resulting rise in pressure may lead to lethargy and eventually coma.

[Top]

High Altitude Pulmonary Edema (HAPE)

This disease may follow AMS, but often it may appear independently. The typical scenario would be a trekker who has no headache or nausea, but finds he has a harder time walking uphill, that he is out of breath on slight exertion compared with the initial days of the trek. There may be a nagging cough and he too may have ascribed these symptoms to a cold. He may be suffering from sub-clinical or early HAPE, a well-recognized entity. With further ascent this may progress to shortness of breath even at rest - descend is now obligatory, or the outcome may be fatal.

Low oxygen causes the pulmonary artery to narrow and this results in exudation of blood near the smaller branches of the lungs (the alveoli). If the exudation continues, blood may escape into the alveoli leading to a cough with watery, blood-tinged phlegm. Such exudation, or "water logging" of the lung tissue interferes further with oxygenation. A popular, compact device called a pulse oximeter can measure the oxygen level in the blood simply and rapidly, using a sensor attached to the index finger. It can be very helpful in confirming if HAPE is present.

[Top]

What is acclimatization?

Acclimatization is a state of physiological "truce" between the body of a visitor and the hostile low-oxygen environment of high altitude. This truce permits the trekker of ascend gradually. (This is distinct from "adaptation" - permanent change to the organism, perhaps over thousands of years, perhaps even at a genetic or evolutionary level, to facilitate survival at altitude. Scientists are trying to decipher if the Sherpas or Tibetans have made such an adaptation.)

For acclimatization to take place the single most important step is hyperventilation- the trekker unconsciously breathes faster and more deeply than normal, even at rest, to make up for the lack of oxygen. However, hyperventilation also leads to loss of carbon dioxide from the blood, making the blood more alkaline, and it turn depressing ventilation. However, 48 to 72 hours after exposure to high altitude, the kidney comes to the rescue and begins to excrete alkali from the blood to restore a more balanced environment in which hyperventilation can continue unabated.

[Top]

Preventing altitude illness

There is little doubt that altitude illness is one hundred percent a preventable illness. No one should die from it. For the past quarter of a century, one of the most important objectives of the Himalayan Rescue Association in Nepal has been to preach the gospel of prevention, from its aid posts in Pheriche (at around 14000ft in the Everest region) and Manang (at around 12000ft in the Annapurna region). There are four golden rules, plus some important general principles that should always be followed:

1. **Understand and recognize the symptoms of AMS**. Recent growth in adventure travel has made trekking at high altitude simpler and more accessible, with the result that more and more people who go trekking are ignorant of the basic facts Of altitude illness.

2. **Never ascend with obvious symptoms.** Incredibly, I have known people who have hired a horse or a yak to go up higher when they were too sick to walk. This is courting disaster.

3. **Descend if symptoms increase.** It is amazing how striking and dramatic the relief may be with even a couple of hundred feet of descent. People with signs of

HAPE or HACE have to descend.

4. **Group m mbers need to look ut for one another** *(perhaps like the buddy system in SCUBA diving).* This rule gets broken with unfailing regularity every trekking season in the Himalayas, because people are just too anxious to complete their trek, even if one of their party members is ill. A trekker with AMS, HAPE Or HACE will want nothing more than to be left alone, unbothered, at the same Altitude- potentially a fatal option. There is no alternative but to bring the person Down to a lower altitude accompanied by a friend who speaks the same language.

Following a conservative rate of ascent

Going too high, too quickly, is the single most important cause of susceptibility to AMS. Beyond about 9000ft, the sleeping altitude should be no higher than about 1500ft from the previous night's altitude. The sleeping altitude, not the altitude achieved during the daytime, is what is important. Altitude sickness often manifests at night because during sleep the oxygen level in the blood may dip further. Many mountain climbers will have been to 14000ft or high in the Alps or in North America but few will have slept at the altitude. In the Himalayas, you don't have to be an experienced climber, or use crampons, to be able to "hang out" at 15000ft or higher for days: easy accessibility to these altitudes makes exposure to AMS also mush easier.

While ascending, every second or third day should be rest day for acclimatization. "Climb high and sleep low" is the dictum, but it is important not to exert oneself excessively in trying to fulfil this.

The trekker should not be in a hurry in the mountains. The itinerary should be planned so that there are enough "leeway days" in case more time is needed to acclimatize. Trying to do a high-altitude two-week trek in one week is always fraught with problems.

Avoiding of excessive exertion in the initial days

Excessive physical exertion at high altitude makes one more susceptible to AMS. It is important to take it easy at high altitude, especially in the initial days. People who are very fit for example marathon runners or those who carry very heavy backpacks seem more vulnerable to AMS than others, probably because they push themselves harder. I once looked after a trekker who felt he could not break his morning jogging sessions despite a strenuous

trek day ahead, even at 4000m! The feeling of" man against nature" may be stronger in this fitter group.

Avoiding alcohol

Jim, a rock star, decided to "whoop it up" with four bottles of beer, on arrival at 3500meters in the Everest region. He felt ill with severe AMS and needed to be helicoptered out two days later. He had been warned not to drink alcohol on the trek, especially while ascending. Alcohol may dehydrate the trekker but more importantly it depresses breathing or ventilation. Sleeping pills may have a similar effect.

Maintaining adequate hydration

Adequate amounts of fluid (about 3 liters a day) are necessary in the mountains:- dehydration mimics altitude sickness and may even predispose to it. On the other hand excessive water drinking should also be avoided as this may lead to electrolyte imbalances.

Maintaining a high carbohydrate diet

A high carbohydrate diet aids ventilation and efficient use of oxygen. The good news is that - in many high altitude places - there is not much alternative: rice, potatoes and other strach-laden foodstuffs tend to be the staple, with not much else to choose from.

Drug prevention (prophylaxis)

Diamox (actazolamide) may be necessary for people going on rescue missions at high altitude or flying in to high altitude cities like La Paz or Lhasa. People with sulpha allergy should not take diamox, the primary drug for prevention, and further details are given below. A second drug, dexamethasone (see below) should also be carried, particularly if the destination is remote: this can be life saving if HACE supervenes.

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TREATMENT

Descent

Wherever, possible this has to be attempted. There is really no magic altitude to descend, but the sick patient may suddenly feel something lift and feel hungry. This is the altitude to which the body is adjusted. Patients with HAPE need to descend slowly and with assistance: excessive exertion even during descent may increase the blood flow to the lungs and exacerbate the problem.

Oxyg n

Lack of oxygen at altitude is the chief reason why people suffer from altitude sickness, so breathing supplemental oxygen is obviously going to make a difference. But oxygen is a hard

commodity to come by in the mountain - cylinders of oxygen are not easily portable. When oxygen available in AMS settings, it should be used.

Drugs

Acetazolamide (diamox): This is the most tried and tested drug for altitude sickness prevention and treatment. Unlike dexamethasone this drug does not mask the symptoms but actually treats the problem. It seems to works by increasing the amount of alkali (bicarbonate) excreted in the urine, making the blood more acidic. Acidifying the blood drives the ventilation, which is the cornerstone of acclimatization.

For prevention, 125 mg twice daily starting the evening before and continuing for three days once the highest altitude is reached, is effective. A recent article in the British Medical Journal suggested taking a higher dosage -- 750mg daily. Our experience in the Indian subcontinent has consistently been that 250 mg per day has been rewarding, while excessive dosage may just increase the side effects.

Side effects of diamox are: an uncomfortable tingling of the fingers, toes and face (called "jhum jhum" in Nepali); carbonated drinks tasting flat; excessive urination; and rarely, blurring of vision. In most of the treks in Nepal, gradual ascent is possible and prophylaxis tends to be discouraged. Certainly if trekkers develop headache and nausea or the other symptoms of AMS, then treatment with diamox is fine. The treatment dosage is 250 mg twice a day for about three days.

Dexamethasone: This steroid drug can be life saving in people with HACE, and works by decreasing swelling and reducing the pressure in the bony skull. The dosage is 4 mg three times per day, and obvious improvement usually occurs within about six hours. Like the hyperbaric bag (See below), this drug "buys time" especially at night when it may be problematic to descend. Descent should be carried out the next day. It is unwise to ascend while taking dexamethasone: unlike diamox this drug only masks the symptoms.

Dexamethasone can be highly effective: many people who are lethargic or even in coma will improve significantly after tablets or an injection, and may even be able to descend with assistance. Many pilgrims at the annual festival at Gosainkunda lake in Nepal suffer from HACE following a rapid rate of ascent, and respond remarkably well to dexamethasone. Mountain climbers also sometimes carry this drug to prevent or treat AMS. It needs to be used cautiously, however, because it can cause stomach irritation, euphoria or depression.

It may be a good idea to pack this drug for a high altitude trek for emergency usage in the event of HACE In people allergic to sulpha drugs (and therefore unable to take diamox) dexamethasone can also be used for prevention: 4 mg twice a day for about three days may be sufficient.

Nifedipine: This drug is generally used to treat high blood pressure, but also seems able to decrease the narrowing in the pulmonary artery caused by low oxygen levels, thereby improving oxygen transfer. It can therefore be used to treat HAPE, though unfortunately its effectiveness is not anywhere as dramatic that of dexamethasone in HACE. The dosage is 20 mg of long acting nifedipine, six hourly.

It can cause sudden lowering of blood pressure so the patient has to be warned to get up

slowly from a sitting or reclining position. It has also been used in the same dosage to prevent HAPE in people with a past history of this disease.

The hyperbaric bag

This is a simple, effective device, made of airtight nylon; it is about 7 feet long ad looks like a long duffel bag. With the patient inside, the bag is inflated with a foot pump until it becomes like a large sausage-shaped balloon. There is a one-way valve to avoid carbon dioxide build up inside, and it has transparent panels to assist communication with its occupant.

The pressure insde the bag is 2 p.s.i,. so the effect is about the same as bringing the patient down a couple of thousand feet. For both HACE and HAPE (but especially, in our experience, for HACE) the changes are usually dramatic within an hour. However there may be a "rebound" tow or three hours after therapy and the patient may need to get in the bag again. Just like the dexamethasone, this bag only helps to "buy tome". Descent is still mandatory as soon as possible.

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Other problems at altitude:-

Periodic breathing

An abnormal breathing pattern whilst asleep is a common occurrence at high altitude: short spells of an increased breathing rate alternate with brief periods when breathing slows down seems to stop the medical term for this is "Cheyne Stokes" respiration. It is only a problem if it makes the suffers wake up repeatedly, breathless, anxious and unable to sleep. An effective remedy is Diamox 125 mg before dinner, which counteracts the low oxygen dips during sleep that trigger the problem. Sleeping pills should be avoided.

Upper respiratory tract infections and symptoms

Many people develop a persistent, bothersome cough and cold-like symptoms in the cold dry air of high altitude. An antihistamine at night like Benadryl 25 mg may help suppress the cough. Antibiotics are sometimes useful, but keeping the head and face covered and breathing through a silk or wool scarf to humidify the air may also help. many studies have shown that upper respiratory tract infections can predispose to AMS.

Peripheral edema

There may be swelling around the eyes, fingers, ankles at high altitude, but this may not indicate AMS per se unless accompanied by the symptoms of AMS. These symptoms without AMS usually require no treatment.

High altitude syncope (fainting): This is well known but harmless problem, in which fainting occurs suddenly, usually shortly after arrival. Simple measures like keeping the individual in a reclining position and raising the legs is helpful.

Travelers with pre-existing health problems; children, and birth control pills

High blood pressure: Blood pressure initially increases at high altitude due to the initial stress of low oxygen triggering neurohumoral changes. However people who suffer from high blood pressure can go up to high altitude as long as this is well controlled and they continue to take their medication.

Coronary heart disease: People with a history of heart attack (moycardial infarction) and even those with coronary artery bypass grafts or angioplasty but with no angina, can trek up to high altitude provided they are fit and able to walk rigorously at low altitude. The high altitude does not seem to add any extra burden to the heart.

Epilepsy: Although seizures may be provoked by altitude there is no convincing evidence that it is unsafe for well-controlled epileptics travelling to travel to high altitude, though such people should always take their anti seizure medications conscientiously.

Migraine: Sufferers may possibly have more attacks in the mountains and this may sometimes be difficult to distinguish from AMS. In doubt it is best to descend.

Lung disease: Also noteworthy is the limited observation that bronchial asthma does not seem to get exacerbated at high altitude due to the cold and exercise. However it is prudent for asthmatics to carry inhalers and other medications. Obviously people with chronic obstructive lung disease may be more short of breath and travel at high altitude would be inadvisable.

Neck surgery and radiotherapy: People with treated cancers like lymphoma or tumors in the neck who have had extensive surgery or radiation treatment may be especially prone to AMS because of damage to the carotid bodies - tiny organs within the carotid arteries that sense oxygen and aid ventilation.

Diabetes: Diabetics on insulin should have a reliable glucometer to check their blood glucose regularly, but high altitude does not seem to cause additional risks.

Corneal surgery: people who have had non laser surgery (radial keratotomy) to correct their short sightedness may run into problems at high altitude due to swelling of their cornea caused by the low oxygen. Such people should carry corrective lenses as well if travelling to high altitude.

Pregnancy: Pregnant women should not sleep higher than 12000ft as this may endanger the fetus; a further problem is that high altitude places are generally remote, making emergencies more difficult to deal with.

Children: Children do not suffer any more from the effect of altitude than adults. However, it is important that a child should be able to communicate any symptoms to responsible adult, so that prompt descent can be arranged. It may therefore be dangerous to take children to high altitude that is not yet old enough to do this.

Contraception: Oral contraceptive pills may predispose to abnormal blood clotting **(thrombosis)** at high altitude. the hypoxia (low oxygen), the excessive red blood cells

(p lycythemia) in the blood, and the possible dehydration in this environment may already be other predisposing factors for thrombosis. Hence it if best to use other forms of contraception at high altitude.

Other dis ase risks

Many high altitude destinations are in developing countries, so it is important to be up to date with **vaccinations** against disease like typhoid and hepatitis, to know about **travelers' diarrhoea** and its treatment, and to understand the other precautions described elsewhere in this book. **Malaria** is not a risk at altitude - transmission does not take place above 2000 meters.

Conditions that mimic altitude sickness

Improving medical facilities in countries such as Nepal have made it much easier to distinguish between altitude illness and conditions that can produce similar symptoms, such as bleeding in the brain (subarachnoid hemorrhage), strokes, dehydration and blood viscosity related problems like venous thrombosis.

Porters in the Himalayas

It is important to be aware that porter may be just as vulnerable to the effects of altitude as tourist; for your own safety, it is also vital to confirm with the trekking agency that your porter has been provided with proper clothing, boots and equipment prior to the start of the trek.

Conclusion

Most of the problems of high altitude are totally preventable. With careful precautions, your experience in the mountains should be safe and rewarding.

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APPENDIX A
ACCLIMATISATION

APPENDIX B
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APPENDIX C
The effects of Altitude on Respiration

APPENDIX D
The first ascent Of Everest Without supplemental Oxygen

APPENDIX E
REFERENCES

Does Altitude training improve endurance exercise performance at sea level?

INTRODUCTION

In the earth's topography, terrestrial elevations above 3048m are considered to be at high altitude.[22, 23] It is common for humans to sojourn to places of altitude and take part in physical exercise, sometimes extensive. Permanent human residence is found as high as 5500m in some parts of South America and Asia (In the Andes & Himalayas).[23] The air pressure in an aircraft cabin is typically equivalent to an altitude of approximately 1500m.[2] The summit of Mt. Everest, the highest point on earth, is 8848m (29.028ft). **Bert, (1878)** showed in a physics study that the effects of high altitude are detrimental to ability to perform physical exercise.[5]

Bert showed that, at altitude, the challenge to athletic performance critically dependant on oxygen for metabolism (i.e. aerobic metabolism) comes not from decreased barometric pressure per se, or from relative changes in gas concentrations in inspired air, but rather from a decrease in ambient partial pressure of oxygen (PO_2) within a reduced barometric pressure at a given altitude.[5] This progressive change in oxygen pressure (both in the environment and in the body) is known as the **Oxygen transport cascade**.[22,25]

Anaerobic performance is not negatively affected at altitude.[19] In fact, it has been shown that performance is enhanced in short-duration, power events such as sprinting, jumping and throwing, due to the decreased air density (resistance) compared to sea level. Furthermore, the force of gravity is reduced with increased distance from the earth's centre.[2] **Dickinson et al (1966)** stated on the basis of ballistic calculations at an altitude corresponding to Mexico city, that a 6cm improvement in the shot put, a 69cm improvement in the javelin, a 53cm improvement in the hammer and a 162cm improvement in the discus could all be expected to be seen.[11] In the 1968 Mexico City Olympics, **Bob Beamon** set a world long jump record, which stood for nearly 25 years.

The formula for ascertaining the partial pressure of inspired oxygen is as follows.

$$\text{Tracheal } PO_2 = (Pbar - 47)20.94x100^{-1}$$

(Where $[PO_2]$ is assumed to be 20.94% of dry air and inspired gas is saturated with water vapour).

PO_2 = partial pressure of oxygen. **Pbar** = barometric pressure.

If a human were to be elevated to a point where Pbar = 47 (19215m) then according to above formula, there would be nothing but water molecules in the trachea![2,5]

Fig 1.0 **Barometric Pressure (standard atmosphere) and equivalent tracheal PO_2 at increasing altitudes**

(Tracheal PO_2 = PO_2 after inspired air is saturated with water vapour at 37°C)

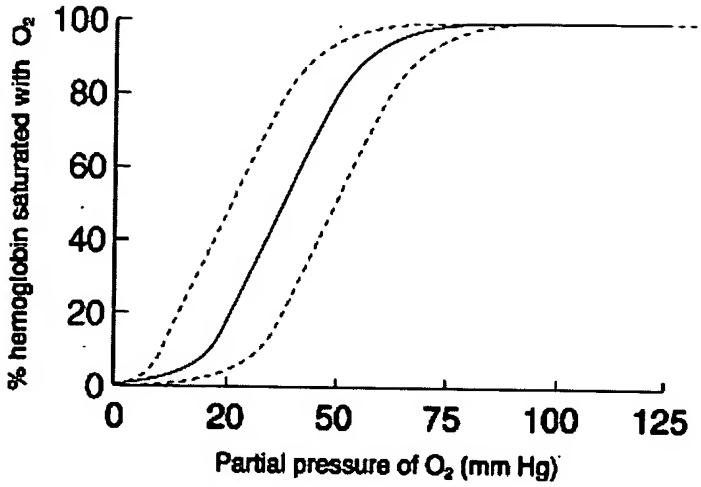
ALTITUDE				ALTITUDE			
m	ft	Pressure mm Hg	PO_2 Tracheal air mm Hg	m	ft	Pressure mm Hg	PO_2 Tracheal air mm Hg
0*	0*	760	149	5500	18050	379	69
500	1640	716	140	6000	19690	354	64
1000	3280	674	131	6500	21330	330	59
1500	4920	634	123	7000	22970	308	55
2000	6560	596	115	7500	24610	287	50
2500	8200	560	107	8000	26250	267	46
3000	9840	526	100	8500	27890	248	42
3500	11840	493	93	EVEREST 8848	29028	232**	38.5**
4000	13120	462	87	9000	29530	230	38
4500	14650	433	81	9500	31170	214	35
5000	16400	405	75	10000	32800	198	32
				19215	63000	47	0

* Taken as sea level

** Subject to fluctuations of approximately +/- 2%, due to weather and environmental factors

Fig 1.1 The Oxyhaemoglobin dissociation curve

The solid line represents O_2 binding affinity to the haemoglobin molecule at standard temperature (37°C) and pH (7.4). The dashed lines represent hypothetical shifts in the curve: to the right with increased 2,3-diphosphoglycerate (2,3-DPG) levels or decreased temperature or pH; to the left with decreased 2,3-DPG or increased temperature or pH [23] (the relationship between 2,3-DPG and altitude acclimatisation is explored in the section on long term adaptations to altitude).



Due to the S-shaped nature of the oxyhemoglobin dissociation curve there is only a small change in % oxygen saturation of haemoglobin (%SaO_2) as altitude increases until an altitude of 3048m is reached. However, aerobic activities are altitude sensitive. In endurance events at the Mexico City Olympics, performance was relatively poor. The winning time in the 10,000m was 2mins slower than the world record. Although haemoglobin is still approximately 90% saturated with oxygen at 1981m (Mexico City is at 2300m) this change is enough to significantly reduce extended aerobic performance.[12] An elevation of 4300m signifies a 32% reduction in aerobic capacity.[4] At 5486m (highest human settlements) %SaO_2 has been shown to be 73%.[30] The PO_2 at this elevation is on the steep part of the curve and further increase in altitude brings about large decreases in %SaO_2. Research has shown that the % SaO_2 at the summit of Everest is 58%[27] (Messner and Habeler ascent of Everest without supplemental oxygen 1978 and 1980) and VO_2 max equivalent of sea level value of a 70-80 yr. old man.[9, 23] An unacclimatised individual on top of Everest would become unconscious and die in 30-40 seconds.[2, 23, 27]

In order to appreciate the benefits of altitude training, it is necessary to understand the mechanisms of human kinetics, the physics of low-pressure environments, and the physiological changes bought about in the body by exposure to altitude.

This work examines the physiological consequences of ascending to altitude, both short and long term, with particular and specific reference to Mt. Everest expeditions (extracts from documented expeditions are contained in the Appendicies). The effect of altitude on aerobic exercise performance is reviewed, and reference made to previous research and athletic events. This review also examines results of earlier scientific studies which have shown that exposure and acclimatisation to altitude, unequivocally benefit aerobic exercise performance at altitude. The question is, do these benefits translate to performance at sea level?

Acclimatisation

For a detailed review of physiological reponses to short and long-term exposure to altitude, refer to appendix A.

There are physiological and metabolic responses to exposure to altitude which improve tolerance to the hypoxia suffered. These responses are broadly termed acclimatisation. Each adjustment to a higher altitude is progressive, and time is required for full acclimatisation.[2, 15, 23] Full adjustment to a moderate altitude equates to only partial adjustment to high altitude. **Levine et al, 1992** stated as a broad guide that it takes 2 wks to acclimatise to altitudes up to 2300m, then 1wk per further 610m up to 4600m.[22] Everest climbers stay at camps 1-3 for 2 months, ascending and descending repeatedly. See appendix C for details on Everest camp elevations. The benefits of acclimatisation are lost within 2-3 weeks upon return to sea level.[6, 12, 14, 26, 30]

Altitude-related medical problems:

For a detailed review of altitude-related medical conditions, and current treatment protocols, refer to appendix B.

Metabolic, Physiological & Exercise capacities at altitude:

Aerobic capacity is not noticeably altered until altitude exceeds 1500m.[8, 26] Thereafter, VO_2max decreases linearly at approximately 10% per 1000m increase in altitude.[8, 23] At an altitude of 6248m, VO_2max is approximately one-half of sea level. Research has shown that for acclimatised men at simulated altitudes approaching the summit of Everest VO_2max was reduced by approximately 70% from 4.13 $L.min^{-1}$ to 1.17 $L.min^{-1}$ (or 49.1 $ml.Kg^{-1}.min^{-1}$ to 15.3 $ml.kg^{-1}.min^{-1}$).[9, 27] These values correspond to an energy power output of approximately 50 $watts.min^{-1}$ on an exercise cycle ergometer.

Even after months of acclimatisation, VO_2max remains significantly below that of sea level. This is because the benefits of acclimatisation are offset by a reduction in circulatory efficiency.[6, 12, 13, 14, 34]

Research has been shown that long-term exposure to altitude induces significant loss in body fat and lean body mass. Moreover, there is a marked increase in basal metabolic rate upon arrival at high altitude.[7, 8, 23]

Altitude training and sea-level performance:

In the 1968 Mexico City Olympics, athletes who resided permanently at altitude did well. Many also excelled at endurance events held at sea level. These triumphs provoked one of the most asked questions in sports science. "Will athletes perform better at sea level as a direct result of training, or being raised at altitude"? As residence at altitude causes adaptations in the oxygen transport chain, it might be expected, if these adaptations last long enough on return to sea level, that they would enhance performance at sea level. **Balke et al (1965)** studied 5 male athletes who trained for 10 days at 2300m. On return to sea level, VO_2max had increased from 3.5L. Min^{-1} to 3.75$L.min^{-1}$. Average times for a 1-mile time-trial run improved from 5.29 mins to 5.13 mins. However, as is obvious from the times, these subjects were not exceptional athletes.[3, 4] **Faulkner et al (1967)** trained 5 athletes for 14 days at 2300m. Sea level results showed an 8.5% improvement in VO_2max as well as improvements in 1 and 2 mile run

times.[12] One of the most well known pieces of research is that of **Daniels and Oldridge (1970)** who trained 6 world-class middle distance athletes at 2300m, exposing them to altitudes of 3000m for several hrs every day.[10] Among these athletes were world record holders, including the then 1500m and mile world record holder, Jim Ryun. 5 of the 6 athletes produced personal bests on return to sea level. After spending an additional 14 days at altitude, Ryun returned to sea level and set a new world record at 1500m.

There are however, several equivocal negative studies. **Buskirk et al (1967)** studied 6 athletes before and after spending 63 days at 4000m. Results showed an unchanged VO_2max and slower running times for the one and two mile events.[6] **Grover and Reeves (1967)** took 5 elite athletes and trained them for 20 days at 3100m. Results showed a decrease in VO_2max in 4 of them on return to sea level.[14]

Aerobic capacity on return to sea level:

When VO_2max is used as criterion, sea level performance is not significantly improved on return from altitude.[3, 4, 6, 12, 23, 39] It can be argued that VO_2max is not a useful performance indicator in these circumstances. Running economy or OBLA (Onset Of Blood Lactate Accumulation) would perhaps be more appropriate. Some of the physiological changes that occur as adaptations to altitude exposure negate adaptations that could conceivably improve performance on return to sea level.[24, 32, 34] The effects of a loss in muscle mass, and a reduced maximum heart rate (HR) and stroke volume (SV) would certainly not enhance performance at sea level.[2, 23] A reduction in cardiac output (Q) would offset any benefits obtained from an increase in red blood cell (RBC) mass. Although circulatory function returns to normal within a few weeks of return to sea level, so do the potentially positive haematological adaptations.[2, 17, 23, 25, 29, 30]

Nutrition at altitude:

Nutrition at altitude can be a major problem. This is more true for individuals at extremely high altitude. With increased altitude, fluid is lost via the respiratory tract.[2, 16, 24] Care should be taken to ensure the individual stays adequately hydrated. Appetite Suppression can be severe during early stages of exposure to altitude. Diets high in Carbohydrates (CHO) and low in salts are well tolerated and beneficial at altitude.[2, 7, 8, 23, 31] More energy is liberated per CHO molecule than per Lipid molecule. (5.0Kcal energy from CHO Vs 4.7Kcal from lipid per litre O_2).[25] Furthermore, high levels of circulating lipid can reduce $\%SaO_2$.[7, 8, 31]

Previous research:

Positive studies such as that of Daniels and Oldridge convinced the athletic community and many coaches that altitude training was beneficial to sea-level performance.[10] As a consequence, altitude training is promoted widely throughout the world. Most previous studies lacked adequate control groups, even the recent ones. **Karvonen et al (1986)** studied 3 elite sprinters for 3wks at 1850m. A control group of 6 similar athletes remained at sea level.[19] With this small number of subjects it is difficult to show significant difference between groups. **Terrados et al (1988)** divided 8 road cyclists into 2 groups. 1 group was studied at sea level, the other for 4wks at 2300m. Results showed a

significant improvement in both groups[36]

There are important variables in study design that may influence the outcome, and therefore the validity of the results. Some of these are as follows.

- For observations to be relevant to performances in top class athletes, the subjects should be top class athletes. It is difficult to conduct research in which the athletes are used as their own controls as they are expected to be in peak competitive condition on two separate occasions within a short timeframe.
- Subjects should be randomly assigned to altitude or sea level training groups.
- The optimal duration at altitude needs to be classified. Two, three, four or more weeks?
- What is the optimal altitude at which training should occur? Below 1800m will not have significant physiological effects. Training above 3000m will decrease performance. It is possible for athletes to become "detrained" while "training" at altitude.
- How long should be left between leaving altitude and competing at sea level?
- What is the optimal pattern for tapering? When, where and for how long should training be decreased prior to competition.
- The need to acclimatise to heat or cold, as well as altitude. This was a particular problem for endurance athletes at the Barcelona Olympics

CONCLUSION

The Mexico City Olympics demonstrated that to perform well in aerobic endurance exercise at altitude, adequate acclimatisation is vital. Better still, be born and raised at altitude. The suggestion that altitude training benefits sea level performance is theoretically sound but remains to be explored fully. There is no unequivocal scientific evidence to either support or refute the claim. Endurance performance requires optimal integration of all aspects of the oxygen transport chain that are stimulated at altitude. If such adaptations occur during altitude training then why do the many studies conducted not reinforce the theory? Is it the result of altitude related reductions in maximum heart rate and stroke volume? Do the previous research shortcomings obscure the answers?

APPENDIX A

ACCLIMATISTION - THE PHYSIOLOGICAL CONSEQUENCES OF ALTITUDE EXPOSURE

The compensatory responses to altitude exposure can be grouped into immediate responses, and long term adjustments.

Immediate Responses

Hyperventilation

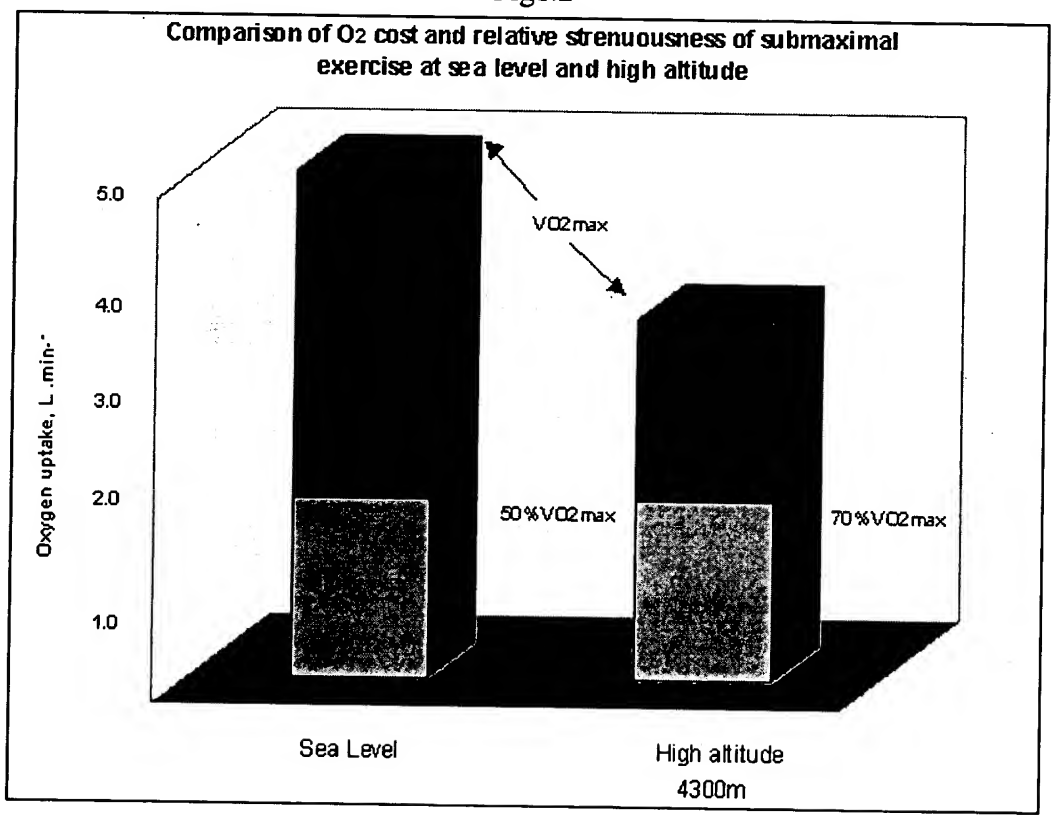
The first and most notable adjustment to exposure to altitude witnessed in the unacclimatised lowlander is Hyperventilation. Peripheral chemoreceptors in the aortic arch and carotid arteries in the

neck are stimulated by a reduction in arterial PO_2 below 60mm Hg. This equates to an altitude of 2000m. Inspiratory activity rate (alveolar ventilation) is increased and alveolar PO_2 rises. Consequently, oxygen loading occurs in the lungs. This process is termed "The Hypoxic Drive". The greater the hyperventilation, the more alveolar air resembles inspired air. Research has shown that mountaineers who respond with a stronger hypoxic drive are better able to perform aerobic exercise at extreme altitudes and can reach higher altitudes than those individuals with blunted ventilatory responses.

Increased cardiovascular response

It has been shown that in the early stages of altitude adaptation submaximal exercise heart rate (HR), systemic arterial blood pressure (BP) and cardiac output (Q) increase by 50%. Increased Q can offset decreased $\%SaO_2$to a certain extent. A 10% increase in Q negates a 10% decrease in $\%SaO_2$.[14, 26, 32, 34, 39]

Fig1.2



The above chart shows the oxygen cost of submaximal exercise at 100 watts on a cycle ergometer remains unchanged at $2.0L.min^{-1}$ at sea level and altitude but relative strenuosness will be higher at altitude (50% VO_2max at sea level = 70% VO_2max at 4300m).[26] The increase in BP has been shown to be related to increase in urinary norepinephrine secretion stimulated by sympathetic nervous system activity. Epinephrine (Adrenaline) levels remain unchanged.[13, 38] In effect, resting HR increases and max HR decreases, moving them closer together.[2, 23, 26]

Longer-Term adjustments to altitude

Hyperventilation and increased submaximal exercise Q enable a rapid adjustment to the challenge of acute hypoxia. There are other, slower acting adjustments that occur with longer stays at altitude.

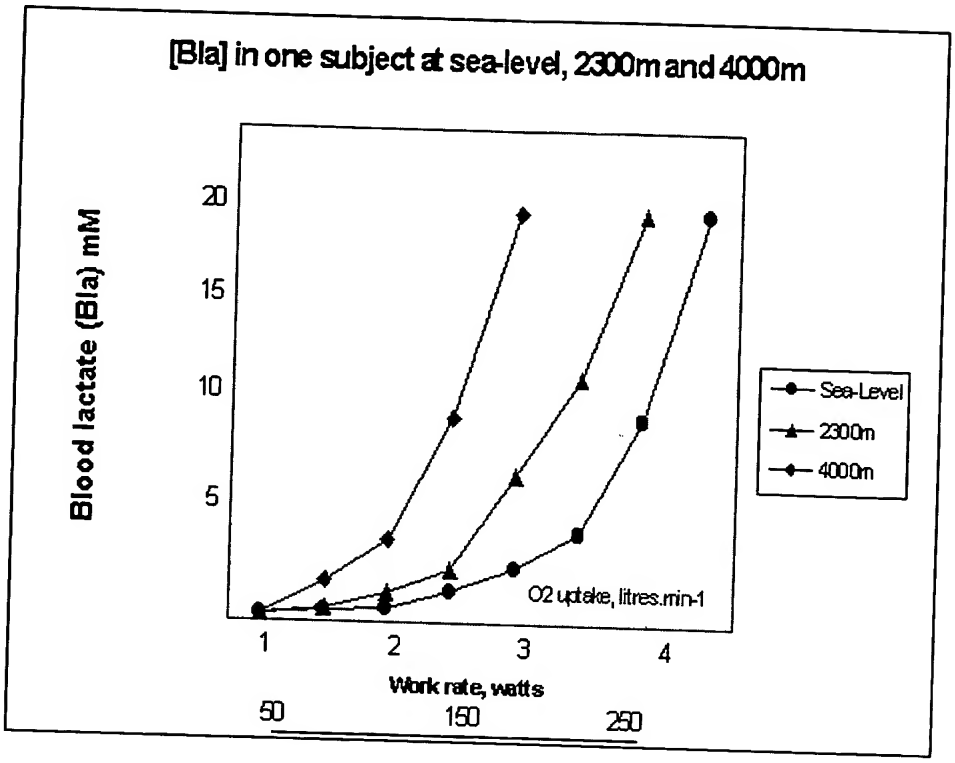
Acid-Base readjustment

Exposure to low PO_2 initiates hyperventilation in an effort to increase alveolar PO_2. This has the effect of decreasing alveolar PCO_2. It has been shown that during prolonged stays at altitude. PCO_2 falls as low as 10mm Hg. CO_2 exists in large amounts in the body as carbonic acid (H_2CO_3). Carbonic acid dissociates into hydrogen ions (H^+) and bicarbonate ions (HCO_3^-). In the pulmonary capillaries, $H^+$and HCO_3^- recombine to form H_2CO_3. Carbonic anhydrase catalyses a condensation reaction producing H_2O and CO_2. The CO_2 then diffuses into the alveoli and is expelled from the body in the form of respired CO_2. The result is increased alkalosis of the blood. This is gradually compensated for by a decrease in blood bicarbonate (achieved by the kidneys excreting base HCO_3^- through the renal tubules) and restoration of a normal pH occurs in an acclimatised person. The restoration of a normal pH increases the responsiveness of the respiratory system and allows ventilation to increase to higher levels, thus adjusting to altitude hypoxia.[2, 18, 23, 25, 26, 32, 38]

"The Lactate Paradox" Reduced Buffering Capacity.

The mechanisms of acid-base readjustment result in a depletion of total body alkaline levels.[2, 25] Consequently, the acid buffering capacity of blood is compromised and the critical level for acid metabolite accumulation (lactate threshold) is lowered. It has been shown that maximum blood lactate (Bla) concentration levels are significantly depressed at altitudes exceeding 4000m.[20,26, 32]

Fig1.3



The occurrence of reduced maximum Bla levels after exercise in acclimatised individuals is termed "The lactate paradox" in as much as hypoxemia associated with high altitude exercise should promote lactate accumulation.[2, 20, 23, 25] This is indicative of anaerobic processes being utilised at lighter work rates at high altitude than is the case at sea level.[2, 13, 20] The reduction in Bla levels is not accompanied by increases in VO_2max or increase in O_2 delivery to exercising muscle groups after acclimatisation. The lactate paradox has been attributed to reduced output of glucose mobilising catecholamines (glucose being the only anaerobic macronutrient) and the lower observed Bla levels to a reduced drive in sympathetic nervous system activity, blunting the capacity for all out effort. It has been shown that reduced Bla levels at high altitude are not due to the decreased buffering capacity of the blood, which occurs after altitude acclimatisation.[20]

Haematological changes

Increases in the blood's oxygen carrying capacity are the most important long-term adaptations to altitude. There are two major ways this is accomplished.

Decrease in plasma volume

Upon exposure to altitude the body's fluid balance is altered due to stimulation of the osmoreceptors, which in turn, stimulate alteration of colloidosmotic pressure.[1]These alterations start within a few days of arrival at altitude and gain momentum over subsequent weeks. The net result is a fluid shift from intravascular space to interstitial and intracellular space, and an overall decrease in plasma volume. This decrease causes the concentration of red blood cells [RBC] in plasma to increase. Research has shown that a 1wk stay at 4300m caused a 25% decrease in plasma volume, a 20% increase in haemoglobin and a 6% increase in haematocrit.[1, 8, 32]$\%SaO_2$ increases significantly above values observed on arrival at altitude. It has been shown that these plasma volume shifts are accompanied by an

increase in diuresis, so osmotic balance is maintained at a lower total body water content in the acclimatised individual.[23, 25, 30, 31, 32]

Increase in RBC mass

The reduced arterial PO_2 concurrent with altitude exposure initiates a condition termed Polycythemia, an increase in total number of Erythocytes.[25] Polycythemia is mediated by erythropoietin (EPO) secreted in response to hypoxia from the kidneys. Erythrocyte production in long bones increases considerably over a course of weeks. Studies have shown that the rate of increase is curved in nature, rapid at first, tapering as time passes.[17, 18, 24, 25, 28, 30] In a 1973 Everest expedition, a 40% increase in haemoglobin and a 66% increase in haematocrit was observed in climbers acclimatised at 6500m.[16, 23] It has been suggested there is an upper limit of [RBC] as increased blood viscosity could hinder blood flow and O_2 diffusion to the exercising cell.[15, 23, 33] Furthermore, links have been suggested between high levels of EPO and pulmonary oedema.[15, 20, 33] Polycythemia directly translates into an increase in the blood's capacity to carry oxygen. Acclimatised climbers have been measured as having a blood-oxygen carrying capacity of 25 to 31ml of oxygen per 100ml of blood compared to 19.7ml in lowland residents.[16, 18] Research has shown that there are markedly fewer haematological changes in women than men during acclimatisation, possibly due to iron-deficiency anaemia (iron is essential to the formation of haemoglobin). Women given iron-supplementation showed higher pre altitude haematocrit and haemoglobin levels than a second non-supplemented group. When their acclimatisation curves were plotted against those of non-supplemented women, it was shown there was a greater haematocrit increase in the supplemented group.[17, 23] Gender differences in acclimatisation is a topic worthy of further research on its own, but these findings generally indicate that athletes of either gender who have borderline iron stores may not respond to acclimatisation as well as those who arrive at altitude with iron reserves adequate enough to sustain an increase in red blood cell production.

Cellular adaptations

Permanent residence and long-term stays at high altitude have significant impact on all aspects of the oxygen transport chain. It has been shown that capillaries are more concentrated in the skeletal muscle of mammals born and raised at high altitude compared to sea level.[37] Furthermore, the activities of oxidative enzymes are enhanced with long-term exposure to altitude.[28, 29, 30] Muscle biopsies from humans residing at high altitude have shown a 16% increase in myoglobin as well as an increase in mitochondria and concentration of oxidative enzymes.[18, 29, 36] These adaptations increase O_2 storage in skeletal muscles. Natives of high-altitude display a shift to the right on the oxyhaemoglobin dissociation curve due to an increase in levels of the compound 2,3 diphosphoglycerate (2,3-DPG). 2,3-DPG binds reversibly with haemoglobin, causing it to have a lower affinity with O_2.[2, 18, 23, 25] The result is an enhanced unloading of O_2 from haemoglobin to the cell. This would place the individual in a physiologically favourable position with regards to performing aerobic exercise at high altitude.[23, 28]

APPENDIX B

Altitude related medical problems

ACUTE MOUNTAIN SICKNESS (15)

The most common form of altitude illness is a constellation of symptoms known as Acute Mountain Sickness (AMS).[15] It is known that exposure to altitude causes AMS, although there are no laboratory tests to identify AMS. Useful clinical criteria are the presence of at least three of the following seven possible symptoms: headache, nausea or vomiting, sleep disturbance, dizziness, shortness of breath, anorexia, and fatigue.

Headache leads the list of complaints, with 70% of visitors above 8000 feet suffer from at least mild headache. 7% of visitors describe severe headache, throbbing and bi-temporal in nature, usually not responsive to over-the-counter medications.

The second most common complaint is sleep disturbance. Over 30% of people going above 8,000 feet note difficulty sleeping. Possibly secondary to periodic breathing (Cheyne-Stokes respiration). This symptom is very disconcerting to the traveller spending the night in a strange hotel room who may awaken with the sensation of not breathing.

Fatigue is the third most common complaint voiced by AMS sufferers. The fatigue is more severe than can be explained by the previously mentioned insomnia, and occurs in 30% of visitors to high altitude.

Shortness of breath and dizziness ensue in equal numbers of patients, both occurring about 20% of the time. Most will notice increased dyspnea with exertion, but dyspnea at rest may suggest increased severity of illness.

$\%SaO_2$ measured by pulse oximetry is a very useful tool in evaluating altitude illnesses. Even though the patient may complain of significant shortness of breath, the SaO_2 is within the normal range or at most minimally reduced. At 9000 feet $\%SaO_2$ measurements between 85-95% are common. Measurements below 85% imply more serious impairment of oxygen exchange than is seen with uncomplicated AMS and should prompt further investigation.

Nausea and anorexia are less common complaints, occurring in less than 5% of cases. This symptom can be merely a loss of appetite or may be severe enough to impair adequate fluid intake. Vomiting indicates more severe illness and also can lead to significant dehydration.

Acute Mountain Sickness has been reported to occur in 17 to 24% of those who travel from sea level to above 8,000 feet. Research has shown that higher altitudes increase the incidence of symptoms with 67% becoming ill at 14,000 feet. The illness usually begins within 4 hours of arrival in 60 % of those affected. On occasion the onset of symptoms may be delayed for two to three days. Onset of symptoms after more than a week should call the diagnosis into question. AMS is generally a self-limited condition spontaneously resolving within three to four days. Still, the patient is often miserable until resolution occurs. The presence of ataxia indicates progression to more serious disease.

The rate of ascent to altitude is an important determining factor in who gets sick. Some may have a predisposition to altitude illness, possiblty connected to low levels of iron, suffering with each visit, though many will not have a recurrence. Predicting who will get sick is not possible. AMS occurs with

equal frequency in males and females, and children often suffer from the malady. Older persons may actually be less likely to develop AMS, perhaps because of reduced activity levels. Excellent physical conditioning does not seem protective.

Various treatments for AMS have been employed in the past, usually based on anecdotal evidence. In studies at high altitude acetazolamide has been reported to be helpful. Acetazolamide is a carbonic anhydrase inhibitor whose mode of action is thought to be increased urinary excretion of bicarbonate resulting in a metabolic acidosis which stimulates respiration. Unpleasant side effects of acetazolamide such as tingling of the fingers and around the mouth and alteration of the taste of carbonated beverages may limit patient acceptance. The incidence of these symptoms may be decreased by prescribing smaller doses than previously recommended. One half of a 250-milligram tablet taken twice a day beginning the day prior to ascent and continued for the first 2-3 days while at altitude is usually adequate. Acetazolamide should not be used by people with a sulfa allergy.

Dexamethasone may act by inducing a non-specific state of euphoria thereby allowing the patient to tolerate uncomfortable altitude symptoms. It does not promote acclimatisation and should be reserved for severe cases until descent is possible. The initial dose is 8 mg. followed by 4 mg. every six hours.

HIGH ALTITUDE PULMONARY OEDEMA [33]

A more severe, potentially life threatening form of altitude illness is High Altitude Pulmonary Oedema (HAPE). HAPE is a non-cardiogenic form of pulmonary oedema occurring with an incidence of less than one percent. For reasons not well understood, some individuals develop severe pulmonary hypertension upon short term exposure to altitude which has been hypothesised to cause a pressure induced fluid leak into the alveolar space of the lung.[2, 15, 23, 25, 33, 38] The flooded capillaries prevent adequate oxygenation and a spiral of worsening hypoxia and increasing pulmonary hypertension ensues. The x-ray picture of HAPE is unilateral or bilateral fluffy infiltrates without enlargement of the heart.

HAPE, unlike AMS, is much more likely to affect young healthy males, with one study reporting a 13-fold increase in risk for that group. Children can and do get HAPE and are susceptible to a peculiar form that strikes the resident of altitude on return from a brief sojourn to lower altitude.

The typical HAPE victim is a healthy male in his twenties who arrives above 8,000 feet and immediately begins heavy physical exertion such as skiing. He may or may not have symptoms of AMS, but within 24-48 hours of arrival begins to develop increasing shortness of breath and a non-productive cough. Believing he has an upper respiratory infection he may try an over the counter cold remedy without improvement. Usually by the third day at altitude the symptoms are severe enough to warrant seeking medical care: significant dyspnea, cough (usually dry but occasionally productive of white or pink frothy sputum), headache, and ataxia. Increasing hypoxia may cloud judgement and unless the victim descends or seeks medical care death may rapidly follow.

Treatment for HAPE is dependent on available facilities and experience. Descent to a lower altitude nearly always brings on dramatic improvement. If descent fails to rapidly improve the patient's condition the diagnosis should be reconsidered. However, descent is not always necessary, provided adequate facilities are available for observation and oxygenation. Many HAPE patients in Summit County, Colorado remain at altitude for treatment, with moderate cases treated with oxygen therapy in the clinic or even the hotel room. A few days of oxygen therapy and rest may allow resumption of recreational activities.

Drug therapy of HAPE has not been very successful. Therapy that works well for other forms of

pulmonary oedema is less effective in HAPE. Diuretics have not proven to be beneficial except in life threatening cases. The use of acetazolamide is not well studied for treatment of HAPE, but theoretical concerns about intravascular fluid depletion because of its diuretic effect suggest it may not be helpful. The recognition that nifedipine effectively decreases pulmonary hypertension thereby decreasing the hypothesised pressure induced fluid leak may allow for improved medical therapy of the disorder. A lightweight portable fabric compression chamber (Gamow bag) allows for simulated altitude descent and can be life saving in instances where actual descent is not possible or oxygen is not available.

HIGH ALTITUDE CEREBRAL OEDEMA(15)

High Altitude Cerebral Oedema (HACE) is a comparatively rare complication of travel to high altitude, but can happen at moderate altitude. It can occur as an isolated entity but may be seen with HAPE. Severe headache, ataxia, and confusion are hallmark symptoms. Lassitude is often such that the patient refuses to move from bed and if left alone may die. This condition increases in incidence with increase altitude but can occur above eight thousand feet. Immediate descent and high flow oxygen are the only known appropriate treatments. Dexamethasone has been suggested as emergency treatment.. Early symptoms are similar to HAPE & AMS, but become severe. Vision disruption, bladder and bowel dysfunction, loss of co-ordination, paralysis on one side, poor reflexes & mental confusion. HACE occurs due to increased intracranial pressure, cerebral vasodilation (see retinal haemorrhaging) and elevated hydrostatic pressure.[2, 15, 16, 23, 25] Extra cerebral fluid distorts brain structures, exacerbates AMS symptoms and increases sympathetic nervous system activity. It can often lead to coma and death. Diagnosis at altitude is difficult. Immediate removal to lower elevation is imperative for treatment.

RETINAL HAEMMORRAGING(35)

Only occurs above 6069m (20000ft). Thought to be due to increase in BP surges from exercise and cerebral vasodilation. Ocular blood vessels dilate from increased cerebral blood flow. and haemorrhage occurs in the macula of eye. Damage can be irreversible

HIGH ALTITUDE SYNCOPE (15)

Recent arrivals to altitude may experience an unexplained syncopal episode. Syncope related to altitude exposure happens within the first 24-48 hours after arrival. Males and females are equally at risk and patients usually deny any prior history of syncope. The syncope appears to be vasovagal in nature and can take place following a meal, after standing up or with exertion. Spontaneous recovery is rapid though the patient may complain of some residual dizziness. The syncope is generally a single episode and the patient may continue the vacation without further concern. Initial reports do not identify a cause of the syncope, and further studies are needed to clarify this issue.

APPENDIX C

The Effects of Altitude on Respiration

Levels of Altitude

Altitude is generally defined on a scale which:

High = 8,000-12,000 ft. (2,438-3,658 meters)

Very High = 12,000-18,000 ft.

Extremely High = above 18,000 ft.

As altitude increases from High to Extremely High, the respiratory system gets pushed to the limit and the body is susceptible to more complications. This is the case in extreme mountain climbing. The following paragraphs will outline various effects of the Everest altitude on the body and minds of climbers. Diary excerpts and actual recorded transcripts from expeditions are included.[21, 38]

Climbing Mt. Everest

The following expeditions are very similar. The path taken by both of the expeditions was up the Southeast Ridge of Everest using similar base camps.

Expedition 1

Rob Hall led this expedition in April of 1996. Unfortunately the expedition ended in tragedy as five members of his team, including him, died during a storm near Everest's summit. Jon Krauker, a surviving member of Hall's team, recounts in his book Into Thin Air the many hardships faced during the climb.

Expedition 2

A year later, David Brashears, a participant of the previous expedition (although not on Rob Hall's Team) led another expedition up Everest. He returned to film an episode for NOVA (Everest: The Death Zone), which explored the effects of altitude on the body and mind.

Base Camp (17,600 ft.)

Both expeditions make several trips ascending and then descending between camps before making a final summit push. This procedure allows the body to acclimatise to the higher altitude.

Expedition 1

Jon Krauker's body had not yet fully acclimatised. He was moving towards Camp I at sluggish pace. For every four to five steps he took, he had to stop, lean against a rope, and take a deep breath.

Expedition 2

Throughout the climb, David Brashears and teammate Dave Carter underwent various cognitive tests at different altitudes. In addition, Brashears used a pulse oximeter to measure his pulse and blood saturation level. At Base Camp, his blood saturation level was 74% (100% is expected around sea level), and pulse was 85 beats per minute (60 per minute at rest is normal for sea level).

Camp I (19,500 ft.)

Expedition 1

Ngawang, a Sherpa*, encountered trouble. He had become delirious, was stumbling, and coughing up pink fluid. He had acquired a severe case of High Altitude Pulmonary Oedema (HAPE). His only chance of survival was rapid descent. However, Ngawang was placed into a Gamow Bag** because rapid descent was not possible at the time. After several days, evacuation helicopters transported Ngawang to a hospital. He later died.

**Sherpa-These are people indigenous to the area around Everest. They always accompany expedition teams in order set up camps and carry supplies.*

*** Gamow Bag-A person displaying symptoms of AMS, HAPE or HACE can be placed into this sealed chamber which resembles an inflatable sleeping bag. The bag is then pumped with air, increasing the concentration of oxygen molecules. Thus, simulating the barometric pressure, and PO_2 of lower altitude. After being enclosed for up to 2hrs, body chemistry homeostasis returns to more normal levels, enabling descent.*

Expedition 2

Brashears' oximeter reading showed 80% saturation level, and pulse of 78. The slight increases in O_2 saturation levels were due to acclimatisation.

Lakba, a Sherpa on the team, was unusually weak. After being examined by an expedition doctor, it was found that his oxygen saturation level was at only 20%. Lakba was quickly placed into a Gamow bag. Later helicopters evacuated him to ground level.

Camp II (21,300 ft.)

Expedition 1

Doug Hansen, a team member of Krauker, lost his voice. After days of breathing the snow-filled air, Hansen's larynx had frozen shut. He continued on the expedition anyway.

Expedition 2

A cognitive test was given to Brashears. He was asked the following question over a phone:

"If Daphne walks twice as fast as Margaret and they are the only two people in the race, who is most likely to finish last"? Brashears answers: "Margaret"

Brashears mental skills were still normal.

Dave Carter's oximeter reading showed a 60% saturation level, and pulse of 140.

Camp III (24,000 ft.)

Expedition 1

Dale Kruse, not on Hall's team, had developed High Altitude Cerebral Oedema (HACE)*. HACE occurs because blood cells in the brain are deprived of oxygen. Suddenly, vessels will leak fluid causing the brain to swell. As a result of the increased pressure in the skull, victims undergo a rapid decline in motor and mental skills. For example, Kruse could not correctly equip himself without help from others. Fortunately, other members his team realised the symptoms and called for an evacuation. After several days at Base Camp, Kruse regained his mental and motor skills.
**HACE does not occur as often as HAPE*

Krauker developed a high altitude cough. Every time he coughed, he was at risk of cracking a rib.

Expedition 2

In a cognitive test, Carter was asked to repeat the following statement:

Statement: "The video camera captured the bank robbers during daylight robbery of the First Avenue Bank"

Carter's Reply: "The video camera captured the daring bank robbers' robbery of the First National Bank. Oh, oh."

Carter's cognitive skills waned in the increased altitude. At his position of elevation, only 35% of the oxygen that is available at sea level was present.

Now Entering the Death Zone

The region above 25,000 ft. is known as the Death Zone. The rate of body deterioration is magnified around this altitude. The process of muscle and weight loss begins in this region. In addition, supplemental oxygen is almost required in order to proceed higher. If supplemental oxygen is not used, the risk for HAPE, HACE, and other sicknesses increases. In the Death Zone, acclimatisation is virtually impossible.

Camp IV (26,000 ft.)

Expedition 1

Krauker's pace was very slow even with the aid of supplemental oxygen*. As Krauker recalled, "I'd take one more step and have to pause for another four heaving breaths and this was the fastest pace I could manage."
**supplemental oxygen at 29,000 ft. gives the feeling of being at 26,000 ft. without oxygen*

Expedition 2

Once again Carter was asked to repeat a sentence.

Sentence: "I'd lived by the river for 20 years, and only twice before in all those years has it been this high."

Carter's Reply: "Ed lived by the river for 20 years, and this was the . . . the first time it had been this

high. Oh, boy . . ."

Brashears' oximeter reading on top of mount Everest showed 78% oxygen saturation in his blood. This relatively high level saturation was obtained through the use of supplemental oxygen bottles.

Even with the oxygen bottles, breathing was still difficult for Peter Hackett, another member of Brashears' team. Peter Hackett attributed this to "The heart rate at rest becoming higher and higher. [At the same time] the maximum heart rate becoming lower and lower, and as you go higher, those two get closer and closer together. [Eventually] You can't do any more physical work."

The Summit (29,028 ft.)

Expedition 1

Krauker reached the Everest summit on the afternoon of May 10, 1996. Unfortunately, his other team members were caught in a storm. The storm caused five deaths and left another team member heavily frost-bitten. Research has shown that one-in-six climbers attempting the summit of Everest die.

Expedition 2

After safely reaching the Everest summit, the team headed back to Seattle to undergo final evaluations. Data collected from the expedition showed, as expected before the expedition, a decline in oxygen saturation with an increase in altitude. Gail Rosenbaum, who was in charge of reviewing the cognitive tests, said in hindsight, "And had we had those numbers [Carter's scores on his altitude tests] available, we would probably suggested that you might not continue."

APPENDIX D

The first ascent of Mt. Everest without supplemental oxygen

"I am nothing more than a single narrow gasping lung, floating over the mists and summits." Reinhold Messner, Everest

Climbing Mount Everest, the tallest mountain in the world, was a challenge that eluded scores of great mountaineers until 1953, when Sir Edmund Hillary and Tensing Norgay first reached its summit. Over the next three decades, more "firsts" followed, including the first ascent by a woman, the first solo ascent, the first traverse (up one side of the mountain and down the other) and the first descent on skis. But all of these climbers had relied on bottled oxygen to achieve their high-altitude feats. Could Mt. Everest be conquered without it?

As early as the 1920s, mountain climbers debated the pros and cons of artificial aids. One, George Leigh Mallory, argued "that the climber does best to rely on his natural abilities, which warn him whether he is overstepping the bounds of his strength. With artificial aids, he exposes himself to the possibility of sudden collapse if the apparatus fails." The philosophy that nothing should come between a climber and his mountain continued to have adherents fifty years later.

In the 1970s, two of its strongest proponents were Reinhold Messner and Peter Habeler. Messner had achieved considerable notoriety by completing a series of spectacular alpine rock climbs without the use of metal protection pegs. In 1974, Messner teamed up with Habeler, a quiet Mayrhofen guide who shared his philosophy, and the pair proceeded to take the climbing world by storm. Agile and slight of build, they scaled the Matterhorn and Eigerwand faces in record time. In 1975, they made a remarkable ascent of the 11th highest mountain in the world, Gasherbrum, without using supplemental oxygen. By 1978, they had set their sights on climbing Mt. Everest -- without supplemental oxygen.

Messner and Habeler quickly found themselves the subject of criticism by members of both the climbing and medical communities. They were labelled "lunatics," who were placing themselves at risk for severe brain damage. The physiological demands of climbing Everest had been studied on previous expeditions, and found to be extreme; in 1960-61, tests conducted on members of an expedition led by Sir Edmund Hillary concluded that oxygen levels at the summit of Mt. Everest were only enough to support a body at rest -- and that the oxygen demands of a climber in motion would certainly be too great.

Despite the controversy, Messner and Habeler continued with their plan. They would climb together with the members of the Austrian Everest Expedition into the Western Cwm, and then make their own separate attempt for the summit. The teams arrived at Base Camp in March of 1978 and spent the next few weeks establishing a secure route through the Icefall, erecting camps I-V and preparing for their ascent.

Messner and Habeler's first attempt began on April 21. They reached Camp III on the Lhotse Face on April 23. That night, Habeler became violently ill with suspected food poisoning. Messner decided to continue his ascent, without his debilitated partner, and set off with two Sherpas the next morning. Upon reaching the South Col, the three climbers were suddenly trapped in a violent storm. They battled temperatures of -40 degrees Fahrenheit and winds of 125 m.p.h. for two full days. Exhausted from struggling with a torn tent and severe hunger, even Messner later admitted to believing his venture was "impossible and senseless." Finally, a break in the weather enabled the shaken party to descend to Base Camp and recuperate.

Messner and Habeler discussed making one more bid for the summit. Habeler had begun to reconsider the use of oxygen, but Messner remained steadfast, declaring that he would not use oxygen -- nor climb with anyone who was using it. He believed that climbing as high as possible, without oxygen, was more important than reaching the summit. Habeler, unable to recruit a new partner, relented, and the two became a team once more.

On May 6, Messner and Habeler set out again. They reached Camp III (7200 meters) easily and, despite a new blanket of heavy snow, felt ready to move on to the South Col the next day. They were now reaching altitudes where they could expect to feel the effects of oxygen deprivation. Messner and Habeler had agreed on carrying two oxygen cylinders to Camp IV, in case of an emergency, and had also made a pact to turn back if either person lost his co-ordination or speech.

The next day, it took them only three and a half hours to reach the South Col (7986 meters), where they camped for the afternoon and evening. Habeler complained of a headache and double vision on the climb up, but felt better after resting, even though both men frequently woke up from their naps gasping for air. They forced themselves to drink tea, hoping rehydration would lessen the effect of the thin air.

At 3 am on May 8, the two woke and began preparing for the day's attempt on the summit.

Simply getting dressed took them two hours. The weather was questionable, but they decided to break camp. Since every breath was now precious, the pair began using hand signals to communicate. Progress was slow. Trekking through the deep snow was exhausting, so they were forced to climb the more challenging rock ridges. It took them four hours to reach Camp V (8500 metres), where they rested for thirty minutes. Even though the weather was still threatening, they decided to continue -- at least to the South Summit, which was 260 vertical metres away.

Messner and Habeler now faced exhaustion unlike any they'd encountered before. Every few steps, they leaned on their ice axes and gasped for breath. Messner described feeling as though he were going to "burst apart." As they climbed higher, they fell to their knees and even lay down in an effort to recover their breath.

Upon reaching the South Summit, the pair roped themselves together and pressed on. The wind battered them about, but they saw a break in the sky and were hopeful that the weather would improve. They had 88.12 vertical meters to go. Messner described a feeling of apathy mingled with defiance. They reached the Hillary step and continued, alternating leads and resting three or four times. At 8800 meters they were no longer roped together, but were so affected by the lack of oxygen that they collapsed every 10 to 15 feet and lay in the snow. Messner testified into his tape recorder that, "breathing becomes such a serious business we scarcely have strength to go on." He described feeling like his mind was dead -- and that it was only his soul that compelled him to crawl forward.

Sometime between 1 and 2 in the afternoon on May 8, 1978, Messner and Habeler achieved what was believed to be impossible -- the first ascent of Mt. Everest without supplemental oxygen. Messner described his feeling: "In my state of spiritual abstraction, I no longer belong to myself and to my eyesight. I am nothing more than a single narrow gasping lung, floating over the mists and summits."

It took Habeler an hour to get down to the South Col, and Messner an hour and three-quarters -- for a distance that had taken them eight hours that very morning. They reached Base Camp, jubilant, two days later.

Messner and Habeler's success puzzled the medical community, and caused a re-evaluation of high-altitude physiology. Messner would return to Mt. Everest in 1980 to successfully complete a solo ascent -- again without supplemental oxygen.

APPENDIX E

REFERENCES

1. **Alexander, J.K.**, et al.: Reduction of stroke volume during exercise in man following ascent to 3100m altitude. J.appl. Physiol:23,849:1967
2. **Astrand P.O**, Rhodal K,: (1986): The textbook of work physiology:3rd edition:McGrwa-Hill: U.S.A
3. **Balke, B.**, F.J. Nagle, J.T. Daniels: Altitude and maximum performance in work and sports activity: JAMA 194: 176-179: (1965)
4. **Balke, B.,** et al.: Variation in altitude and its effects on performance. In Exercise physiology. Edited by H.B Falls. New York, Academic press, 1968
5. **Bert, P.**,"La Pression Barométrique," Masson et Cie, Paris: 1878

6. **Buskirk, E.R.**, Kollias, J., Akers, R.F., Prokop, E.K., Reategui, E.P.: Maximal performance at altitude and on return from altitude in conditioned runners.: J. appl, physiol., 23:259-266: 1967
7. **Butterfield, G.**,(1990): Elements of energy balance at altitude. In Hypoxia: The adaptations, J.R. Sutton., G. Coates., J.E. Remmers., (Eds), B.C Decker Inc., Toronto, pp.88-93.
8. **Butterfield, G.E.**, Gates, J., Fleming, S.I., Brooks, G.A., Sutton J.R., Reeves, J.T. Increased energy intake minimizes weight loss in men at high altitude. J. Appl. Physiol., 72: 1741-1768
9. **Cymerman, A.**, et al.: Operation Everest II: maximal oxygen uptake at extreme altitude. J. appl. Physiol. 66: 2446-2453: 1989
10. **Daniels, J., Oldridge, N.**: The effects of alternate exposure to altitude and sea level on world-class middle distance runners. Med. Sci. Sports 2:107-112: 1970
11. **Dickinson, E.R.**,et al: Project Olympics, schw. Zschr. Sportsmed.:14:305: 1966.
12. **Faulkner, J.A.**, Daniels, J.T., Balke, B.: The effects of training at moderate altitude on physical performance capacity. J. Appl, Physiol; 23:85-89: 1967
13. **Green, H.J.**, et al, : Operation Everest II: Muscle energetics during maximal exhaustive exercise. J. Appl, Physiol: 66: 142-150: 1989
14. **Grover, R.F.**, Reeves, J.T. Exercise performance of athletes at sea level and 3100m altitude. In The effects of altitude on physical performance, R.F. Goddard (Ed), Athletic institue, Chicago, pp. 80-87
15. **Hackett, P.H.**, Rennie R.,Grover,. J. Reeves: .Acute mountain sickness and the edemas of high altitude: A common pathogenesis?: Resp, Physiol.,46(3):383: 1981
16. **Hackett, P.H.**, et al,. Physiology of man on the summit of Mt. Everest: J. Physiol., 334:99: 1983
17. **Hannon J.P.**, et al.: Effects of altitude acclimatisation on blood composition of women. J. Appl, Physiol., 26:540: 1969
18. **Hoppeler, H.**, Desplanches, D., Muscle structure and modifications in Hypoxia., Int. J. Sports Med., 13:166-168: 1992
19. **Karvonen, J.**, Saarela, J., The effect of sprint training performed in a hypoxic environment on specific performance capacity., J. sports Med., 26:219-224: 1986
20. **Kayser B.**, et al.,: Maximal lactate capacity at altitude: Effect of bicarbonate loading., J. Appl, Physiol., 75:1070: 1993
21. **Krakauer, J.**, Into Thin Air. New York:U.S.A: Villard Publishing.1st Edition :1997
22. **Levine, B.D.**, Stray-Gunderson, J., A practical approach to altitude training: where to live and train for optimal performance enhancement. Int. J. Sports Med. 13: 209-212: 1992
23. **McArdle,W.D.**, Katch, F.I., Katch, V.L:1996: Exercise physiology: 4th Edition: Williams & Wilkins. U.S.A
24. **MacDougall, J.D.**, Green, H.J., Sutton, J.R., Coates, G., Cymerman, A., Young, P., Houston, C.S., Operation Everest II: Structural adaptations in skeletal muscle in response to extreme simulated altitude. Acta. Physiol. Scand. 142: 421-427: 1991
25. **Marieb, E.M.** 1996: Human anatomy and physiology: 4th edition: Benjamin Cummings science publishing. U.S.A
26. **Pugh, L.G.C.E.**, Athletes at altitude., J. Physiol. 192:619-646: 1967
27. **Pugh, L.G.C.E.**, Muscular exercise on Mt. Everest. J. Physiol (Lond)., 141:233 :1958
28. **Rahkila, P.**, Rusko, H., Effect of high altitude training on muscle enzyme activities and physical performance characteristics of cross-country skiers. In Int. series on sports sciences, P.V Komi (Ed) Exercise and sport Biology. Vol 12. Champaign, IL: Human Kinetics Books, pp 143-151: 1982
29. **Reynafarje, C.**: Myoglobin content and enzymatic activity of muscle and altitude adaptation., J. Apply. Physiol., 17:301: 1962
30. **Reynafarje, C.**: Haematologic changes during rest and physical activity in man at high altitude. In The Physiological effects of high altitude. Edited by W.H. Weihe. New York, Macmillan, 1964.

31. **Rose, M.S.**, et al., Operation Everest II: Nutrition and body composition. J. Appl. Physiol. 65:2545-2551: 1988
32. **Saltin, B.**, Cardiovascular & Pulmonary adaptation to physical activity. In Exercise, Fitness and Health., C, Bouchard., R.J shephard., T. Stephens, J.R Sutton, B.D. McPherson (Eds). Champaign, IL: Human Kinetics Books, pp. 187-203: 1988
33. **Schoene, R.B.**: High-Altitude Pulmonary Edema: The disguised Killer, Phys. Sportsmed., 16:103: 1988
34. **Sutton, J.R.**,et al: Operation Everest II: Oxygen transport during exercise and extreme simulated altitude. J. Appl. Physiol. 64:1309-1321: 1988
35. **Sutton, J.R.**: High altitude retinal haemorrhage. Sem Resp.Med., 5:159: 1983
36. Terrados, N., Jansson, E., Sylven, C., Kaijser, L., Is Hypoxia a stimulus for synthesis of oxidative enzymes and myoglobin?: J. Appl. Physiol 68: 2369-2372: 1990
37. **Valdivia, E.**, Total capillary bed in striated muscle of guinea pigs native to peruvian mountains. Am. J. Physiol., 194:585, 1958
38. **Ward, M. P.**, Milledge, J. S., & West, J. B.: High Altitude Medicine and Physiology 2nd edition: New York: Chapman & Hall Medical.: 1995.
39. **Wolfel, E.E.**, et al., Oxygen transport during steady state, submaximal exercise in chronic hypoxia. J. Appl. Physiol., 70:1129-1136: 1991

HOME

Respiration

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(presented by Saint Michael's College, Colchester, VT, USA)

Do you like to breathe? Well, we do, and we learned a whole lot about how it works in mammals and in other groups of animals. If you'd like to know more, take a breather and enter our website. Just sit back, relax, take deep breaths, and inhale all of our information. Go for it!

What is respiration? Why do animals respire and why is it important?

Respiration is the process by which animals take in oxygen necessary for cellular metabolism and release the carbon dioxide that accumulates in their bodies as a result of the expenditure of energy. When an animal breathes, air or water is moved across such respiratory surfaces as the **lung** or **gill** in order to help with the process of respiration. Oxygen must be continuously supplied to the animal and carbon dioxide, the waste product, must be continuously removed for cellular metabolism to function properly. For example, if this does not happen and carbon dioxide levels increase in the body, pH levels decrease and the animals may eventually die (see Question: Why is the regulation of body pH important?).

Oxygen is valuable because it is important in many ATP-producing cycles occurring throughout the body such as, the Krebs cycle, and the electron transport chain. Glycolysis breaks down glucose, a six-carbon sugar, into the three-carbon molecule of pyruvic acid. The series of reactions associated with glycolysis are necessary for anaerobic and aerobic pathways to work, and are also the most fundamental in cellular metabolism. In the presence of 0_2, the pyruvic acid, which came about from the breakdown of glucose, is further oxidized. However, under anaerobic conditions the pyruvic acid is reduced to lactic acid. Glycolysis follows a specific pathway and ultimately, the oxidation of 1 mol of glucose to pyruvic acid ends in a net gain of only 2 mol of ATP and 2 NADH molecules.

The Krebs cycle is a series of eight major reactions following glycolysis. In these reactions, acetate residues are degraded to CO_2 and H_2O. With each turn of the Krebs cycle, 2 CO_2 molecules and 8 H^+ atoms are removed. These hydrogen atoms, which are removed two at a time, are transported by NADH and $FADH_2$ and further go into the electron transport chain.

The electron transport chain, also known as the respiratory chain, oxidizes the NADH and $FADH_2$ from the Krebs cycle to H_2O by oxygen. This cycle involves electrons that move through about seven steps in order of their decreasing electron pressures, more specifically, from the high **reducing potential** of NADH to $FADH_2$ to oxygen, the final electron acceptor. The electron transfer is the final pathway for all electrons during aerobic metabolism, and it uses the energy from the transfer for the phosphorylation of ADP to ATP. A total of 38 ATP molecules are collectively released from the three cycles of glycolysis, the Krebs cycle, and the electron transport chain working together. Without oxygen, the Kreb's cycle and electron transport chain would be disabled and only 2 ATPs would be produced by glycolysis. To maintain an adequate supply of oxygen to cells, animals must have an efficient means of gas transfer and respiration.

What is oxygen debt?

In some animals, such as mammals, if the supply of oxygen to active muscle cells is not sufficient to produce enough ATP to maintain intense activity, the only source of additional ATP will be from glycolysis. Without sufficient oxygen, some of the pyruvic acid produced is reduced to lactic acid, which accumulates in the tissues, resulting in fatigue. Excess lactic acid may also enter the blood, decreasing blood pH and affecting other tissues in the body. When muscle activity decreases, extra oxygen is needed to convert the lactic acid back to pyruvic acid, which is then utilized by the Kreb's cycle. This extra oxygen represents the animal's oxygen debt. Some animals, such as the goldfish and some intertidal invertebrates, can avoid oxygen debt through the use of biochemical pathways that convert lactic acid to alcohol, which can then be excreted.

What is the difference between air and water as respiratory environments? How does this affect the amount of energy spent obtaining oxygen in water and air and therefore the structures used in ventilation?

Water and air are radically different as respiratory environments in a number of ways. The most significant difference is that water contains only 1/13 as much O_2 as air does, or 1% to 21% (water to air) by volume. Water also is over 800 times denser than air and 50 times more viscous, so aquatic breathers must use more energy to simply move water across their respiratory surfaces. Fish, for example, use as much as 10% of the oxygen they take in to provide breathing muscles with enough oxygen to burn the energy needed to keep water passing over the gills in the right direction. Humans use only 1-2 % of their oxygen intake to keep breathing. Temperature also has an effect on the amount of oxygen each environment can hold. As water temperature increases the amount of dissolved oxygen decreases. Air also shows a slight reduction in oxygen content with increasing temperature, but it isn't physiologically significant because there is so much oxygen in air to begin with. Gas diffusion rates are also lower in water than in air. Salt water contains less oxygen than fresh water because the higher salt concentration decreases gas solubility. All of this produces a vast difference between aquatic and terrestrial organisms in the amount of energy expended to obtain oxygen.

How is oxygen carried through the blood and passed onto other cells? What role does hemoglobin play in oxygen transfer? What conditions affect hemoglobin/oxygen affinity?

Hemoglobin (Hb) is found in red blood cells, being the principle part of a **red blood cell**. Hemoglobin is a large protein with four **polypeptide chains** and four **heme groups**. Each heme group has an iron atom attached to it, which is where oxygen attaches to be carried to cells and tissues. It is important to note that the O_2/Fe bond, that is initially made so the oxygen can be transported, can be readily broken in the right conditions. These conditions are altered depending on if oxygen needs to be picked up or released to tissue cells. The reason hemoglobin is found in red blood cells only is that the conditions needed for efficient oxygen transport by the Hb molecules can be quickly changed, and all of this can be done without changing the conditions throughout the body. Some of the conditions necessary for oxygen and carbon dioxide transport may be unsuitable for other reactions that need to take place throughout the body, so keeping Hb within the red blood cells allows oxygen transport to occur without interfering with other bodily functions. Conditions that control the ability of hemoglobin (Hb) to bind to oxygen include

the partial pressure of O_2 in the surrounding respiratory medium (air or water), temperature, pH, CO_2 levels. A high partial pressure of O_2 in the surrounding respiratory medium will increase the rate at which the O_2 diffuses into the blood. Hemoglobin's affinity for oxygen typically decreases if temperature increases, pH decreases, or CO_2 levels increase.

There are a few different kinds of hemoglobin, all doing the same job, but each having its own affinity to O_2. Normally hemoglobin will pick up an O_2 when the partial pressure of the O_2 in the blood (O_2 dissolved in solution) is high, and there are fewer than 4 O_2 molecules on the hemoglobin, 4 being the maximum number able to be carried. When an O_2 molecule is attached to a hemoglobin molecule it is not affecting the partial pressure of the O_2 in the blood, as there is a low concentration of O_2 in the **blood plasma**, just not enough to supply the cells of the body. The best scenario for oxygen transfer from the lungs to body cells and tissues is hemoglobin to have high affinity at the respiratory surface (high amount of O_2 diffusing across the lung surface) and low oxygen affinity (give the oxygen away) near body cells that need it (low O_2 content).

Other factors that affect hemoglobin/oxygen affinity include a decrease in pH, which reduces hemoglobin/oxygen affinity (the Bohr effect). A decrease in pH reduces Hb/ O_2 affinity because the shape of the oxygen-binding sites of the hemoglobin molecule changes, making it more difficult for them to bind to oxygen. (See "Why are red blood cells important to carbon dioxide transport?" for a complete explanation of the mechanisms involved). A rise in body temperature reduces Hb/O_2 affinity as the increased energy (heat) will prevent bonds from forming or break bonds currently in place. Increased CO_2 content can affect the affinity because CO_2 can bind to sites where O_2 would normally bind. Hemoglobin normally picks up CO_2 at the tissues and releases it at the respiratory surface in exchange for oxygen to complete the chain. When the concentration of CO_2 is too high it takes the place of oxygen on Hb at higher than normal rates.

Oxygen dissociation curves graphically represent the percent of hemoglobin's oxygen binding sites that are holding oxygen at different partial pressures of oxygen. The sigmoid (S-shaped) curve is due to subunit cooperativity between the four oxygen binding sites on a hemoglobin molecule. When no binding sites are occupied by oxygen, it is relatively difficult to get the first oxygen to bind. After it does, however, the structure of the hemoglobin molecule is altered a bit, and the second binding site becomes more accessible. This makes it a bit easier for the second molecule of oxygen to bind. After this, additional oxygen molecules bind rather easily to the third and fourth binding sites. Therefore, oxygen binds slowly at first, and then more quickly, giving the dissociation curve a sigmoid shape.

How is carbon dioxide transported in the blood?

The transportation of carbon dioxide is a very significant process of the gas-transfer systems within many animals. There are three main ways in which CO_2 is transported in the blood. A small percentage of the CO_2 that is in the blood is dissolved molecular CO_2. A larger amount of CO_2 reacts with $-NH_2$ groups of hemoglobin and other proteins to form carbamino compounds. However, most of the CO_2 that is transported in the blood is in the form of bicarbonate (HCO_3^-). In general, CO_2 is diffused into

the blood from the tissues. The blood transports CO_2 to the respiratory surfaces of the lungs or gills, where it is released into the environment. The blood mainly consists of plasma and erythrocytes (red blood cells). Most of the CO_2 entering and leaving the blood does so through erythrocytes.

Why are red blood cells important to carbon dioxide transport?

Most of the CO_2 entering or leaving the blood go through red blood cells for two reasons. One reason is due to the enzyme **carbonic anhydrase**. This enzyme is present in red blood cells and not in the plasma. The enzyme is important in the transportation of CO_2 because, within the red blood cells, it catalyzes the reaction of CO_2 with OH^- resulting in the formation of HCO_3^- ions. As the level of HCO_3^- ions increases within the erythrocytes, the HCO_3^- ions diffuse through the erythrocyte membranes into the plasma of the blood. In order to maintain electrical balance within the erythrocytes, an anion exchange occurs in a process called a **chloride shift**. In this process, HCO_3^- ions leave the red blood cells while a net influx of Cl^- ions from the plasma enters the red blood cells. The membrane of red blood cells is very permeable to both ions because the membrane has a high concentration of a special anion carrier protein, the **band III protein**. This protein allows for a **passive diffusion** of the Cl^- and HCO_3^- ions to and from the red blood cells and plasma. This keeps the bicarbonate from building up in the red blood cells, which would slow down or stop the reversible conversion of CO_2 to HCO_3^-. **Facilitated diffusion** occurs in the movement of CO_2 across the respiratory surfaces as bicarbonate (HCO_3^-) diffuses out of the red blood cells and into the epithelium where it is converted back to CO_2. Excretion of CO_2 is limited by the rate of bicarbonate-chloride exchange across the erythrocyte membrane.

The second reason why most of the CO_2 is transported to and from the blood by passing through the erythrocytes is that O_2 binds to Hemoglobin (Hb) at the respiratory surface, causing hydrogen ions (H^+) to be released. The increase in H^+ ions combines with HCO_3^- to form CO_2 and OH^-. Thus, more CO_2 is formed and can leave the blood across the respiratory surface. Excess H^+ binds to OH^-, forming water and allowing the pH to increase enough to promote the binding of oxygen to Hb. The release of O_2 from Hb in the tissues makes the Hb available to bind to H^+, promoting the conversion of CO_2 to HCO_3^-, which helps draw CO_2 from the tissues. Therefore, CO_2 that is being transported into and out of the red blood cells minimizes changes in pH in other parts of the body because of proton binding to and proton release from hemoglobin, as it is deoxygenated and oxygenated, respectively (Figure 1.).

Figure 1.

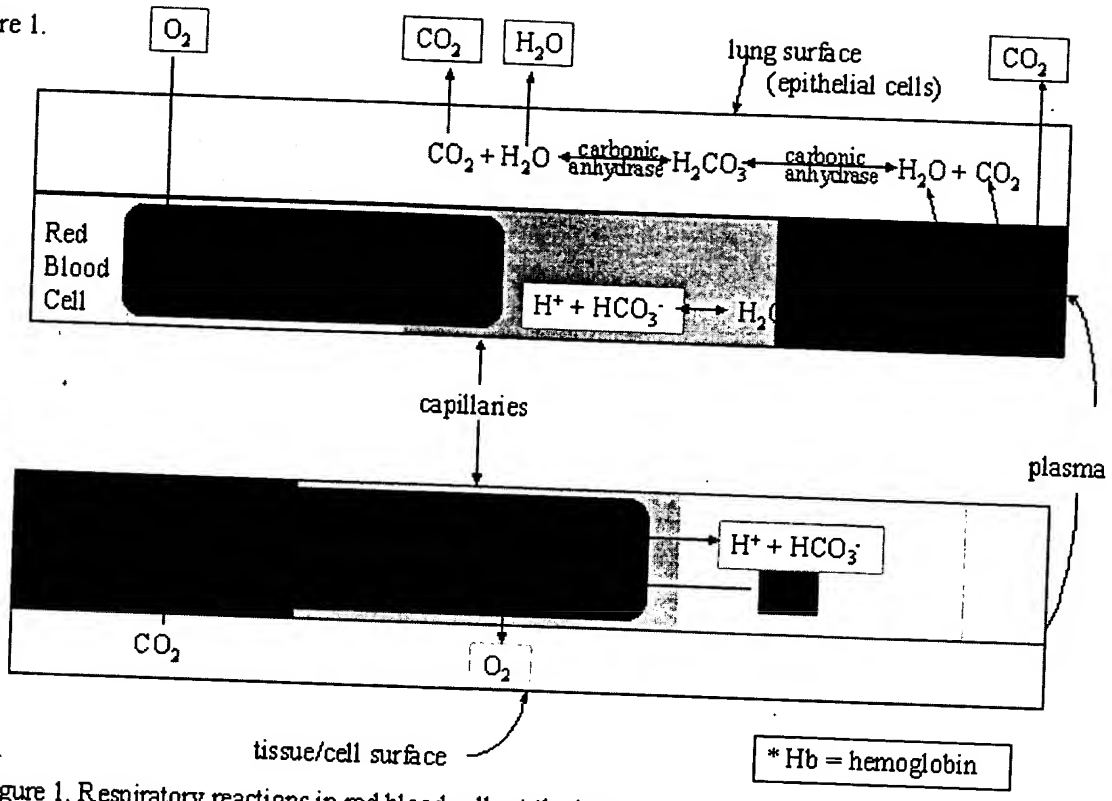

Figure 1. Respiratory reactions in red blood cells at the lung surface and the cell/tissue surface.

Designed by: J. Bailey

Why is the regulation of body pH important?

The regulation of body pH is important because some organs, tissues, and various types of cells are more affected by changes in pH than others. Therefore, within an animal's body are various mechanisms, including mechanisms at the cellular level, that regulate the body pH in order for the animal to maintain normal bodily functions. For example, the regulation of body pH is needed in animals in order to stabilize volume of hydrogen ions and to regulate enzyme activity. Within cells, pH is regulated in order for cellular functions to proceed. At the tissue level, the body has the ability to redistribute acid between body compartments because some tissues have the ability to tolerate much larger fluctuations in pH than others do. In general, animals have a body pH that is on the alkaline side of neutral, which means that there is less hydrogen than hydroxyl ions in the body. Human blood plasma, at 37° C (normal body temperature) has a pH of 7.4. Normal functioning can be maintained in mammals at 37° C over a blood plasma pH range of 7.0-7.8.

How does breathing regulate pH?

One of the main ways that a mammal regulates pH is through the control of respiration. For example, if the body pH in a mammal decreases, the respiration rate and depth of respiration increases in order to

get rid of the excess CO_2, which brings H^+ levels back down and brings pH back up. Hence, when breathing is increased, CO_2 levels in the blood decline and pH increases. If pH increases, respiration rate decreases, thereby increasing CO_2 levels, which forms more carbonic acid and brings pH back down.

In mammals, a stable body pH is achieved by adjusting the release of CO_2 through the lungs and excretion of acid or bicarbonate through the kidneys, so that acid excretion and production are balanced. The collecting duct of the mammalian kidney has acid-excreting and base-excreting cells, which can be altered to increase or decrease acid or base excretion. In aquatic animals, the external surfaces have the capacity to extrude acid in similar ways to the collecting duct of the mammalian kidney. For example, a protein ATPase exists in the skin of frogs and gills of freshwater fish which excretes protons on the apical surface of the epithelium. Fish gills also have a HCO_3^-/Cl^- exchange mechanism, which aids in the regulation of body pH.

What are alkalosis and acidosis, and what are the consequences?

When an animal's body experiences changes in its body pH, many physiological changes occur within the body of the animal. When there is excessive alkalinity in the body and therefore an increase in body pH, this is referred to as alkalosis. Conversely, when there is excessive acidity in the body and therefore a decrease in body pH, this is termed acidosis.

In terms of the effects of pH on the respiration of animals, when lung **ventilation** is decreased causing CO_2 excretion to drop below CO_2 production, body CO_2 levels rise and pH falls. This is referred to as **respiratory acidosis**. When lung ventilation is increased causing CO_2 excretion to rise above CO_2 production, body CO_2 levels fall and pH rises. This is referred to as **respiratory alkalosis**.

It is important to know that body fluids are electroneutral, which means that the sum of the anions equals the sum of the cations. Respiratory acidosis and alkalosis disturb the electroneutrality of the body fluids. However, at the cellular levels, the pH is regulated and electroneutrality is brought back to the body fluids. There are various mechanisms, which regulate cellular pH and thus maintain electroneutrality in the body fluids.

One cellular mechanism involves proteins and phosphates within the cell that act as physical **buffers** to regulate cellular pH. The most important buffers in the blood are proteins, especially hemoglobin, and bicarbonate because the CO_2-to-bicarbonate ratio can be adjusted by excretion of CO_2 in order to regulate pH.

A second mechanism that regulates cellular pH involves the important reaction of HCO_3^- with H^+ ions. For example, when oxygen enters red blood cells within the blood, the molecules attach to the hemoglobin thus releasing H^+ ions. The pH decreases, which increases cellular acidity and causes the reaction of HCO_3^- with H^+ ions to form CO_2. The CO_2 then diffuses out of the red blood cells thus regulating the pH within the cells.

Also the proton-exchange and the anion-exchange mechanisms in the cell membrane play important roles in adjusting cellular pH. For example, if a cell is acidified, there is a H^+ efflux, which is connected

to a Na^+ influx and there is a HCO_3^- influx, which is connected to Cl^- efflux. This mechanism adjusts the pH of the cell to a less acidified state. Lastly, another mechanism for regulating cellular pH involves the simple passive diffusion or **active transport** of H^+ ions from the cells.

What are the organs that facilitate gas exchange/respiration?

Gas transfer occurs by passive diffusion from the environment across the body surface. Air breathing, in most vertebrate animals, involves the movement of air into and out of the lungs. Insects have developed a very different method of gas transfer between the tissues and the environment and this includes a tracheal system. Water breathing, on the other hand, for most aquatic animals involves a unidirectional flow of water over the gills. Thus, the structure and design of the mammalian, insect, and fish respiratory systems are radically different. Each gas-transfer system is built according to the needs of the animal and to the medium in which it lives.

In air breathing animals, the related respiratory organ that facilitates gas transfer, is the lung. The lungs in air breathing vertebrates are large organs of respiration located in the chest cavity. In humans, the right lung is made up of three lobes and the left lung is composed of two lobes. They are suspended in the pleural cavity and opens to the outside by the **trachea**. The respiratory portion of the lung includes the terminal bronchioles (under glossary term as **bronchus**), the respiratory bronchioles, and the **alveolar ducts and sacs**.

In contrast, the associated respiratory organs of the fish include the gills. The gills consist of a feathery, branched tissue richly supplied with blood vessels. The gills facilitate the exchange of oxygen and carbon dioxide with the surrounding water.

Most insects respire by means of a tracheal system. In this system, gas is directly transported to the tissues by air-filled tubules that bypass blood. The pores to the outside, called **spiracles**, deliver the gases of respiration. The drawback of this system is that the gases diffuse slowly in the long narrow tubules; as a result, these tubes need to be limited in size for adequate gas transfer. The advantage is that O_2 and CO_2 diffuse much faster, 10,000 times faster, from the air than in water, blood, or tissues. This feature often uses less energy for ventilation and bypasses the need for a circulatory system. Another advantage of the tracheal system is that oxygen can be delivered directly to tissues that need it, such as flight muscles.

What are the components of the mammalian lung?

The mammalian lung is more complex than that of the amphibian, reptile, or other non-mammal species, and consists of a complex network of tubes and sacs. To be more specific, the human respiratory system consists of the nasal cavity, **pharynx**, trachea, bronchi, and lungs. Although not considered a part of the respiratory system, the ribs, muscles, and diaphragm are important and help in the expansion and contraction of the lung. To begin with, the pharynx and larynx lead to the lungs; the larynx is connected to the trachea, which branch into the right and left bronchi. These bronchi further divide and lead to the terminal bronchioles. The terminal bronchioles continue and then lead air to the respiratory bronchioles. The respiratory bronchioles themselves connect to a fan of alveolar ducts and sacs. The function of the alveolar ducts and sacs is to moisten and cleanse the air taken in, and furthermore, transfer it to the gas-

exchanging portion of the lung. These alveolar ducts and sacs are filled with many capillaries, the smallest of the blood vessels, and also consist of connective tissue fibers.

Alveoli, millions of interconnected sacs, also make up a large part of the lung. The human lung is made up of an average of 300 million alveoli. Through diffusion, gases from the air in the alveoli are exchanged with the gases in the pulmonary capillary blood. The transport of gases depends on this exchange and relationship between O_2 pressure in the alveoli and the surrounding atmospheric pressure.

As seen, through a series of branches and smaller ducts, air is delivered to the respiratory portion of the lung (the terminal bronchioles, respiratory bronchioles, and the alveolar ducts and sacs); gas is transferred across the respiratory epithelium in these specific areas. Gas transfer also occurs across **acini** and the **pores of Kohn**, which allow for collateral (side-by-side) movement of air.

How do different animals ventilate their lungs/spiracles? (mammals, birds, reptiles, frogs, invertebrates)

The functional anatomy of the lungs and associated structures vary considerably among animals in the mechanism of lung/spiracle ventilation.

Mammals

The lungs of mammals are elastic, multi-chambered bags, which open to the exterior through a single tube, called the **trachea**. The lungs are suspended within the **pleural cavity**. The ribs and the **diaphragm** form the walls of the pleural cavity, which are referred to as the **thoracic cage**. The thoracic cage mostly consists of the lungs, but between the lungs and the thoracic walls there is a low-volume of pleural space sealed and fluid filled.

During normal breathing, the thoracic cage expands and contracts by a series of skeletal muscles, the diaphragm, and the **external and internal intercostal muscles**. The respiratory center within the **medulla oblongata** controls the contractions of these muscles through the activity of motor neurons. During inhalation, the volume of the thorax increases due to the lowering of the diaphragm. In addition, the ribs are raised and moved outward by the contraction of the external intercostal muscles. The increase in thoracic volume reduces **alveolar pressure**, and air is drawn into the lungs. During exhalation the diaphragm and external intercostal muscles relax, reducing the thoracic volume. Reducing the thoracic volume raises alveolar pressure and forces air out of the lungs.

Birds

In the lungs of birds, gas exchange occurs in air capillaries extending from parabronchi, a series of small tube-like structures, which are functionally equivalent to the **alveoli** in mammals. The parabronchi extend between large dorsobronchi and ventrobronchi, both of which are connected to an even larger tube, the **mesobronchus**. The parabronchi and connecting tubes form the lung, which is contained within a thoracic cavity. However, the volume of the thoracic cage and lung changes very little during breathing and therefore, are not directly involved in avian lung ventilation. In birds, the **air-sac system** connected to the lungs ventilates the avian lungs. During inspiration, air flows through the mesobronchus into the caudal air sacs. Air also moves through the dorsobronchus and the parabronchi into the cranial air sacs. Oxygen is then diffused into the air capillaries from the parabronchi and is taken up by the blood. During expiration, air leaving the caudal air sacs passes through the parabronchi and

then through the mesobronchus to the trachea. The cranial air sacs, during expiration, move air through the ventrobronchi to the trachea and into the environment. The bird ventilation mechanism is special because birds are capable of flying at high altitudes while maintaining a sufficient supply of O_2 in their bodies. Specifically, the unidirectional flow of air through the parabronchi aids in increasing the efficiency of gas exchange within the avian lungs thus giving birds the capability of flying at high altitudes. This means of gas exchange is more efficient that thet tidal flow model seen in mammals.

Reptiles

The ribs of reptiles form a thoracic cage around the lungs. During inhalation, the ribs moving cranially and ventrally, enlarging the thoracic cage. This process reduces the pressure within the cage below atmospheric pressure. The **nares** and **glottis** open and air flows into the lungs. Exhalation occurs passively by the relaxation of the muscles that enlarge the thoracic cage, which release energy stored in stretching the elastic component of the lung and body wall.

In tortoises and turtles, the ribs are fused to a rigid shell. Outward movements of the limb **flanks** and/or the ventral part of the shell and by forward movements of the shoulders are what inflate the lungs. The reverse process results in lung deflation, involving the retraction of limbs and head into the shell leading to a decrease in pulmonary volume. Therefore, when a turtle is withdrawn into its shell, its lungs are deflated and the turtle can't breathe.

Frogs

In frogs, the nares open into a **buccal cavity**, which is connected through the glottis to a pair of lungs. During inhalation, air is drawn into the buccal cavity with the nares open and the glottis closed. Then the nares close and the glottis is opened. The buccal floor then rises, forcing air from the buccal cavity into the lungs. This lung-filling process may be repeated several times in sequence inhaling air in portions. This same process may also occur during expiration in which the lungs release air in portions. Inhaling and exhaling air in portions may produce a mixture of pulmonary air low in O_2 and high in CO_2. This complex method of lung ventilation may be to reduce fluctuations in CO_2 levels in the lungs to stabilize and regulate blood P_{CO2} and control blood pH. Frogs also exchange gasses across their skin, so the lungs are not the only repsiratory surface.

Invertebrates

Invertebrates have a variety of gas-transfer mechanisms. In some invertebrates, ventilation does not occur. These invertebrates rely on diffusion of gases between the lung and the environment. Spiders have ventilated lungs called "book lungs". The lungs have respiratory surfaces consisting of thin, blood-filled plates that extend like the leaves of a book into a body cavity guarded by an opening (spiracle). The spiracles open and close to regulate the rate of water loss from these "book lungs". Snails and slugs also have ventilated lungs in which their lung volume changes enabling them to emerge from and withdraw into their rigid shells. In aquatic snails the lungs serve to reduce the animal's density. Most insects have a gas-transfer mechanism called the tracheal system (to know more information on the insect tracheal system, link to the questions: How do insect tracheals work? How are they different from lungs and gills?)

How do gills work?

For most fish species gills work by a unidirectional flow of water over the **epithelial surface of the gill**, where the transfer of gases is made (O_2 in, CO_2 out). The reason for this unidirectional flow of water, and not an inhaling and exhaling of water, is due to the energetics of the system. The energy that would be required to move water into and out of a respiratory organ would be much more than that used to move air because water is more dense and **viscous**.

The blood flowing just under the epithelial gill tissue usually moves in a countercurrent flow to that of the water moving over it. This allows for the most O_2 to be taken in by the blood because the **diffusion gradient** is kept high by the blood picking up oxygen as it moves along, but always coming in contact with water that has a higher O_2 content. The blood receiving the O_2 will continue to pick up O_2 as it moves along because fresh water is being washed over the epithelial lining of the gills. An important aspect to remember here is that the water going over the gills needs to be moving unidirectional, either by the fish forcing the water to move in one direction or if the water is moving mostly in one direction.

There are two ways fish ventilate their lungs: buccal/opercular pumping (active **ventilation**) and ram ventilation (passive ventilation). The fish pulling in water through the mouth (buccal chamber) and pushing it over the gills and out of the opercular chamber (where the gills are housed) accomplishes buccal/opercular ventilation. The pressure in the buccal chamber is kept higher than the pressure in the opercular chamber so the fresh water is constantly being flushed over the gills. A fish swimming with its mouth open, allowing water to wash over the gills accomplishes ram ventilation. This method of ventilation requires fast water or a fast fish to keep enough oxygen going to the gill surface.

How do insect tracheoles work? How are they different from lungs and gills?

Insect tracheal systems are a series of air filled tubes that run from the edge of the **exoskeleton** to the cells/tissues far within the body. The tracheal system terminates at the **tracheoles**, that often go in between or right into cells to deliver O_2 very close to the **mitochondria**. There is usually fluid between the terminal ends of the tracheols and the body cells, but as the insect becomes more active the fluid is replaced by air so gas exchange is heightened. The use of tracheal systems is superior to using water or blood as mediums of gas exchange because O_2 and CO_2 diffuse 10,000 times more rapidly in air so the necessary gases can be exchanged more quickly. However, there is a size limit for effective ventilation via a tracheal system, which is one reason that insects cannot grow to gargantuan sizes.

The inner wall surface of the tracheal system is made of the same material that composes the exoskeleton, which helps to prevent water loss. Spiracles, the openings to the outside air, can be opened and closed at will to in regulate air exchange, water loss, and to keep out debris.

Ventilation is usually accomplished through convection, the mass movement of gases. Some larger insects can compress and expand their body wall to coincide with the opening and closing of spiracles to pull air in and push air out. To reduce the amount of energy used in respiration some insects use the discontinuous ventilation cycle (DVC) which is composed of open, closed, and intermediate flutter phases. During the closed phase (spiracles closed) the O_2 that is in the body is being used more rapidly than the CO_2 being produced. Due to this, when the open phase begins there is a **O_2 gradient**, the low end being within the body, forcing a rush of O_2 from the surrounding air into the spiracles and releasing any CO_2 that was produced. This process may be helped along by the expansion of respiratory sacs within the body to pull more air in or push more air out. During the flutter phase there is rapid inhalation

and exhalation. This type of ventilation uses the most energy and it is not understood why it is done.

What is the role of pulmonary surfactants in respiration?

Pulmonary surfactants are **lipoprotein** complexes produced in the lungs that are used to reduce the effort in breathing and help prevent the collapse of **alveoli**. Pulmonary surfactants make expansion of the alveoli easier by lowering the **surface tension** that holds membranes of different alveoli together and minimizes expansion of individual alveoli. This makes it easier for alveoli membranes to slide against each other when they are expanded to take in air.

Surfactants also reduce the chances of alveolar collapse by stabilizing surface tension when an alveoli sac is expanded. When alveoli are expanded the surfactant is spread out more, which increases surface tension. Surface tension is a major contributor to wall tension, which determines if a small alveolar sac collapses into a larger alveolar sac. Collapse occurs when the pressure inside a small alveolar sac (wall tension in relation to the radius of the sac) is greater that the pressure in a larger alveolar sac, forcing the air in a small sac (high pressure) to force its way into the large sac (low pressure). The surfactant prevents this by minimizing the surface tension, which minimizes the difference in wall tension and thereby minimizing the pressure difference between alveoli.

How are breathing patterns controlled or regulated?

Breathing is an automatic and rhythmic behavior regulated by several nerve centers in the brain, more specifically, in the neurons of the **pons** and **medulla oblongata**. The central processing of many sensory inputs control breathing movements. The central processor is made up of a *pattern generator* and a *rhythm generator*. From these, the depth and amplitude of each breath is controlled and the frequency of breathing is controlled, respectively.

Ventilation helps maintain satisfactory rates of gas transfer and blood pH levels. Breathing movements with eating, talking, or other bodily functions are controlled by sensory inputs as well. The muscles and diaphragm help ventilate the lungs. This action is stimulated by the spinal motor neurons and the phrenic nerve that get information from the neurons that make up the medullary respiratory centers. The muscles of the respiratory system are finely controlled, and this allows humans to breathe, sing, and whistle. The medullary respiratory center also contains inspiratory and expiratory neurons. The activity of the inspiratory neurons correspond to inspiration. The networks of neurons connect to higher brain centers, the **chemoreceptors** and **mechanoreceptors**.

Neuronal action has much to do with breathing and respiratory activity. From the **phrenic nerve** or from individual neurons in the medulla, scientists have been able to record inspiratory neuronal activity and learn more. Inspiration is characterized by a changing release of medullary neurons. The activity recorded shows a rapid onset, a gradual rise, and an abrupt termination with a sudden burst of activity related to inhalation. Following this activity, the inspiratory muscles contract and intrapulmonary pressure decreases. Inspiratory neuronal activity can be said to depend on the cycle of various neurons-inspiratory, early inspiratory, off-switch, post inspiratory, and expiratory neurons. The "off-switch" neurons come about at the sharp cutoff point in the activity of inhalation, and also when neuronal activity has reached a threshold level. Pulmonary **stretch receptors** that are stimulated by lung expansion decrease the threshold level. Without these receptors working on the inspiratory neurons,

there would be over-expansion of the lung. At the beginning of expiration, the amount of work by the inspiratory muscles begins to decrease, which is caused by the post-inspiratory neurons. The post-inspiratory neurons are responsible for slowing the rates of expiration. At the end of the post-inspiratory activity, the expiratory neurons are then released.

The time between each breath is determined by the interval between the bursts of activity of the inspiratory neurons. The interval between a burst of activity is related to the amount of activity in the burst that came before it, as well as with nerves in the pulmonary stretch receptors. If the activity of inspiration is great, as is when taking a deep breath, there is a longer interval between inspirations. This allows the ratio of duration on inspiratory and expiratory activity to stay constant no matter how long the breath taken is. The pulmonary stretch receptors can influence this ration, however, depending on their activity. If these receptors are very active, the duration of expiration may be extended, leaving a longer time for exhalation. This can occur during expiration when the lung empties out slowly and when the pulmonary stretch receptors are still active while the lung stays inflated.

Expiratory neuronal activity appears not to influence normal exhalation. Exhalation most often occurs passively, as the thoracic cavity relaxes after inhalation. Expiratory neurons are used for forced exhalation, however, and are only active when the inspiratory neurons are still.

The human respiratory system has the ability to adjust its breathing patterns to different environments and to disturbances in breathing, such as asthma (a narrowing of the airway which causes breathing difficulties). This flexibility is due to a number of sensors found throughout the body, which send signals to the respiratory networks in the brain. The chemoreceptors detect any changes of acidity that may occur in the cerebral spinal fluid (CSF) in the brain, or in blood. For example, when P_{CO2} levels increase in the body, the levels of pH in the CSF decrease. The chemoreceptors act to drive ventilation, and the amount of breathing is increased. The mechanoreceptors of the body help maintain any expansions of the lung and also help maintain the size of the airway.

How does an animal respond to extreme conditions?

Animals have the ability to respond to extreme conditions, such as reduced oxygen levels (hypoxia), increased carbon dioxide levels (hypercapnia), diving, and exercise. As we will see, each of the extremes mentioned will induce a respiratory response specific to its demands.

Decreased O_2 levels (hypoxia)

In aquatic environments, gas mixing and diffusion occur less rapidly than in air. Because of this, aquatic animals experience frequent changes in O_2 levels and face regions of hypoxia. CO_2 levels may or may not come about with different O_2 levels.

Some animals can survive periods of hypoxia. To do so, the animals either use anaerobic pathways, or will adjust their respiratory and cardiovascular systems in order to deliver oxygen throughout their bodies while experiencing reduced O_2 availability.

In air, the levels of O_2 and CO_2 can remain relatively stable. There is, however, a decrease in O_2 levels with higher altitudes. With increasing altitude, there is a gradual reduction in P_{O2}, and each animal has a

different way of fighting these conditions. For example, and increase in blood levels of 2,3 DPG will decrease the affinity of Hb for O_2, thereby releasing more O_2 for the tissues to use.

A decrease in P_{O2} of the air will cause a decrease in blood P_{O2}. The carotid and aortic bodies are stimulated when this happens, causing an increase in lung ventilation. When there is an increase in lung ventilation there is more CO_2 eliminated and a reduction in blood P_{CO2} as well. As a result, the pH of the CSF rises and tends to reduce ventilation. When an animal is in an area of hypoxia for a longer period of time, blood and CSF pH levels are brought back down to normal by the release of bicarbonate in the body. For instance, for a human who has moved to a higher altitude, this process takes about one week. The **carotid bodies** and the **aortic body** chemoreceptors may be reset to the lower CO_2 levels. Hypoxic conditions cause a vasoconstriction in the pulmonary capillaries and a rise in pulmonary blood pressure. This circulates the blood away from the poorly ventilated areas of the lung.

There are other effects to living in such an extreme condition. Humans, for example, tend to be smaller in size, barrel chested, and have an increased lung volume. There is a reduction in limb development and often excessive growth or development of the right ventricle, due to increased pulmonary blood pressures. Also, over long periods of time, most animals will increase the number of red blood cells and the amount of **hemoglobin** in the blood. This feature increases the oxygen capacity of the blood. If there is a decrease in O_2 levels in the blood, erythropoietin, a hormone of the kidney and liver, is produced. This hormone stimulates red blood cells are production in bone marrow. Hypoxia may also result in systemic vasodilation, as well as an increased cardiac output. When O_2 supplies are restored from increased hemoglobin levels in the blood and through ventilation, cardiac output is brought back to normal.

Increased CO_2 levels (hypercapnia)

P_{CO2} represents the amount of CO_2 in solution. When there is an increase in blood P_{CO2}, there is an increase in ventilation. The aortic and carotid body chemoreceptors, the mechanoreceptors in the lungs, and most especially, the central H^+ receptors, regulate this activity. They do so by sending messages to the respiratory center of the brain. The pH of the CSF is brought back to normal levels in order to bring ventilation levels back to normal as well. When there is an increase in CO_2 levels, there is a distinct increase in ventilation. After the stress of increased CO_2 levels is relieved, ventilation gradually returns to a level slightly above the ventilation level that occurred before hypercapnia. The reason it returns to a level only slightly above the initial ventilation volume relates to a rise in plasma and CSF bicarbonate levels. As a result of the increased plasma and CSF bicarbonate, pH levels are brought back to normal, even though there may still be a high level of CO_2.

Diving by air-breathing animals

During a dive, animals are subjected to periods of hypoxia. Anoxia, severe hypoxic conditions that can result in permanent damage, is a large problem for a mammal's central nervous system (CNS) and because of this, oxygen must be continuously supplied to the animal. Throughout a dive, animals combat anoxia by making use of oxygen stores in the lungs, blood, and tissues. Animals that dive have higher hemoglobin levels, which increase the oxygen capacity of the blood, and also have larger oxygen stores in muscle (**myoglobin**) to efficiently supply the body with O_2. In order to utilize the stores efficiently during a dive, blood is delivered to the brain and heart first. The tissues and organs to where blood did not go to resort to an anaerobic pathway. As a result, the heart rate slows and cardiac output

decreases. The O_2 stores need to be large enough to sustain aerobic metabolism because diving animals cannot tolerate the large buildup of lactic acid from anaerobic metabolism.

During a dive, inspiration is prevented and water is detected from receptors found near the glottis, mouth, or nose. Although there is an increase in CO_2 levels and a decrease in blood pH, ventilation is prevented. This is because the carotid and aortic body chemoreceptors are not acted upon by the respiratory neurons to cause ventilation.

One potential danger of a prolonged dive is that gases in solution in the blood under the higher pressure of greater depth may come out of solution too quickly and form air bubbles in the blood vessels when the pressure diminishes. In humans, this can cause a condition known as "the bends", in which gas bubbles accumulate in the joints, and can even obstruct blood flow in small vessels in the brain and other parts of the body. Many diving mammals prevent this condition by exhaling when they dive, thereby emptying most of the air out of their lungs. In addition, under the pressure of diving, the alveoli collapse, thereby forcing air into the bronchioles, where it cannot go into solution in the blood.

Exercise

During exercise, more oxygen is needed, and more CO_2 and metabolic acid are produced. In addition, there is an increased cardiac output because the tissues need more oxygen supplied to them. This is also caused due to an increase of lung ventilation to support gas tensions in arterial blood, which experiences faster blood flow. When an individual is exercising, the venous blood shows signs of decreased O_2 levels, increased CO_2 levels, and an increase in H^+ levels. In the arterial blood, however, the average P_{O2} and P_{CO2} do not differ much as they do in the venous blood, except when under extreme exercise. When exercise has stopped, there is a decrease in the amount of breathing and eventually, a decline in ventilation volume as well once the balance between O_2 consumption and CO_2 production is restored and the O_2 needs are met. This may take a while, if a significant oxygen debt has been built up by a prolonged period of anaerobic muscle activity.

What are some of the physiological problems associated with high altitude?

Altitude Sickness, and the related disorders and symptoms, pose an immediate threat to athletes who spend their time exercising at high altitudes. The most commonly affected athletes are high altitude mountain climbers. It is not uncommon to find them above 20,000 feet using skill, strength and concentration to scale some of the most dangerous mountains our Earth has to offer. Unfortunately, the challenge of high altitude mountaineering also brings with it the risk of serious illness and possibly death. Why is this? Why does our body respond so negatively to high altitude environments?

Increased altitude is coupled with decrease atmospheric pressure meaning that for every breath inhaled; there is less O_2 available. Think of breathing inside a bedroom filled with 1000 liters of O_2. There is plenty of air around you and the pressure is high, like it is at sea level. Now imagine you are breathing in a warehouse that is filled with an equal amount of air. The decreased in pressure would make it harder to breathe. The atmospheric pressure on top of Mt. Everest (29,028 ft) is 33% less than it is at sea level.

This means that 66% less oxygen is available. This is what climbers face when performing at high altitudes.

Due to the oxygen constraint, our bodies are forced to work harder to continue to metabolize. Respiration must increase to get sufficient oxygen across the lungs. Increasing our respiration can be taxing to our systems. If the body overdoes it, Acute Mountain Sickness (AMS) can occur. This is the result of increased respiration and circulation. The body overcompensates for the decreased oxygen by sending too much to the brain. Leakage into the brain occurs and causes swelling. Decreased oxygen also starves nerve cells, triggering the release of adenosine. This chemical decreases the body's metabolism, decreasing our need for oxygen. It also dilates blood vessels into the head and neck, which allows more oxygen to go to the brain. This is the same dilation that is correlated with migraine headaches. A common treatment for the migraine symptoms is the use of caffeine. Caffeine blocks the adenosine receptors, thus preventing vasodilatation. If AMS goes unnoticed, a more serious sickness can occur. High Altitude Cerebral Edema (HACE) has occurred from 10,000 ft. and above. It occurs when AMS is overlooked and thus brain swelling increases. In extreme cases, death can result. The symptoms of HACE are imbalance, severe headache, vomiting, nausea, and hallucinations. Known treatments include rapid descent, supplemental oxygen, water, and a diuretic called Diamox. Victims of HACE often experience comas and death. The increased blood flow, as a result of high altitude that was mentioned before, can also lead to High Altitude Pulmonary Edema (HAPE). This occurs when excessive blood pressure causes fluid to leak from the blood vessels into the alveoli sacs of the lungs. Cases have been seen at 8,000 ft. and above and were characterized by difficulty breathing, gurgling sound in lungs, fever, coughing, and exhaustion. The fluid in the lungs blocks the oxygen-blood interface. The body compensates by increasing heart rate and blood pressure, thereby forcing more fluid into the lungs. Eventually, if altitude is not decreased, the victim drowns. No oxygen reaches the lung/capillary interface.

Other problems associated with high altitude include Periodic Breathing and Khumbu Cough. In Periodic Breathing, during sleep above 14,000 ft., climbers will repeatedly stop breathing, gasp, hyperventilate, and then stop again. The medulla of the brain is affected causing breathing to become irregular. CO_2 builds up, the sleeper hyperventilates, CO_2 decrease, respiration stops, and the cycle continues. The body actually responds to a state of alkalosis, which causes the shut off of breathing. Khumbu Cough is commonly seen with high altitude climbing. It is characterized by a dry cough that results from too high a breathing rate. The mucosa of the bronchi dries out due to the increased breathing rate and contact with dry, cold air. Besides irritation, the Khumbu Cough can result in broken ribs as a result of severe coughing episodes. The only prevention is to keep the breathing rate down. This reduces the drying out of the mucosa.

1: N Engl J Med. 1991 Oct 31;325(18):1284-9.

Comment in:

- N Engl J Med. 1991 Oct 31;325(18):1306-7.

Prevention of high-altitude pulmonary edema by nifedipine.

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BACKGROUND. Exaggerated pulmonary-artery pressure due to hypoxic vasoconstriction is considered an important pathogenetic factor in high-altitude pulmonary edema. We previously found that nifedipine lowered pulmonary-artery pressure and improved exercise performance, gas exchange, and the radiographic manifestations of disease in patients with high-altitude pulmonary edema. We therefore hypothesized that the prophylactic administration of nifedipine would prevent its recurrence. METHODS. Twenty-one mountaineers (1 woman and 20 men) with a history of radiographically documented high-altitude pulmonary edema were randomly assigned to receive either 20 mg of a slow-release preparation of nifedipine (n = 10) or placebo (n = 11) every 8 hours while ascending rapidly (within 22 hours) from a low altitude to 4559 m and during the following three days at this altitude. Both the subjects and the investigators were blinded to the assigned treatment. The diagnosis of pulmonary edema was based on chest radiography. Pulmonary-artery pressure was measured by Doppler echocardiography and the difference between alveolar and arterial oxygen pressure was measured in simultaneously sampled arterial blood and end-expiratory air. RESULTS. Seven of the 11 subjects who received placebo but only 1 of the 10 subjects who received nifedipine had pulmonary edema at 4559 m (P = 0.01). As compared with the subjects who received placebo, those who received nifedipine had a significantly lower mean (+/- SD) systolic pulmonary-artery pressure (41 +/- 8 vs. 53 +/- 16 mm Hg, P = 0.01), alveolar-arterial pressure gradient (6.6 +/- 3.8 vs. 11.8 +/- 4.4 mm Hg, P less than 0.001), and symptom score of acute mountain sickness (2.0 +/- 0.7 vs. 3.9 +/- 1.9, P less than 0.01) at 4559 m. CONCLUSIONS. The prophylactic administration of nifedipine is effective in lowering pulmonary-artery pressure and preventing high-altitude pulmonary edema in susceptible subjects. These findings support the concept that high pulmonary-artery

pressure has an important role in the development of high-altitude pulmonary edema.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial

MeSH Terms:

- Adult
- Altitude Sickness/etiology
- Altitude Sickness/prevention & control*
- Blood Pressure/drug effects
- Delayed-Action Preparations
- Female
- Human
- Male
- Middle Age
- Mountaineering*
- Nifedipine/administration & dosage
- Nifedipine/therapeutic use*
- Pulmonary Artery/drug effects
- Pulmonary Artery/physiopathology
- Pulmonary Edema/diagnosis
- Pulmonary Edema/etiology
- Pulmonary Edema/prevention & control*
- Support, Non-U.S. Gov't

Substances:

- Delayed-Action Preparations
- Nifedipine

PMID: 1922223 [PubMed - indexed for MEDLINE]

☐ 1: Respiration. 1997;64(6):435-43.

Related Articles, Links

High altitude pulmonary edema.

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Altitude, speed and mode of ascent and, above all, individual susceptibility are the most important determinants for the occurrence of high-altitude pulmonary edema (HAPE). This illness usually occurs only 2-5 days after acute exposure to altitudes above 2,500-3,000 m. Chest radiographs and CT scans show a patchy predominantly peripheral distribution of edema. Wedge pressure is normal at rest, and there is an excessive rise in pulmonary artery pressure (Ppa) which precedes edema formation. Bronchoalveolar lavage in patients with advanced HAPE shows evidence of inflammatory response with increased capillary permeability. There are, however, no prospective data indicating whether the inflammatory response is a primary cause of HAPE or a consequence of edema formation. Excessive rise in Ppa appears to be a crucial pathophysiologic factor for HAPE. Recent observations of high Ppa in HAPE-susceptible subjects who did not develop pulmonary edema after rapid ascent to high altitude suggest either that Ppa does not necessarily reflect capillary pressure in these individuals or else that additional factors, such as an inflammatory response and/or a decreased fluid clearance from the lung, are necessary for the development of pulmonary edema. The treatment of choice is immediate descent. When this is impossible and supplemental oxygen is not available, treatment with nifedipine is recommended until descent is possible.

Publication Types:
- Review
- Review, Tutorial

MeSH Terms:
- Altitude*
- Capillary Permeability
- Hemodynamics
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- Inflammation Mediators/physiology

- Pulmonary Alveoli/metabolism
- Pulmonary Edema/etiology
- Pulmonary Edema/physiopathology*
- Vasoconstriction

Substances:

- Inflammation Mediators

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☐ 1: J Am Coll Cardiol. 2000 Mar 15;35(4):980-7.

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Stress Doppler echocardiography for identification of susceptibility to high altitude pulmonary edema.

Grunig E, Mereles D, Hildebrandt W, Swenson ER, Kubler W, Kuecherer H, Bartsch P.

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OBJECTIVE: This prospective single-blinded study was performed to quantitate noninvasive pulmonary artery systolic pressure (PASP) responses to prolonged acute hypoxia and normoxic exercise. BACKGROUND: Hypoxia-induced excessive rise in pulmonary artery pressure is a key factor in high-altitude pulmonary edema (HAPE). We hypothesized that subjects susceptible to HAPE (HAPE-S) have increased pulmonary artery pressure response not only to hypoxia but also to exercise. METHODS: PASP was estimated at 45, 90 and 240 min of hypoxia (FiO2 = 12%) and during supine bicycle exercise in normoxia using Doppler-echocardiography in nine HAPE-S and in 11 control subjects. RESULTS: In the control group, mean PASP increased from 26+/-2 to 37+/-4 mm Hg (deltaPASP 10.3+/-2 mm Hg) after 90 min of hypoxia and from 27+/-4 to 36+/-3 mm Hg (deltaPASP 8+/-2 mm Hg) during exercise. In contrast, all HAPE-S subjects revealed significantly greater increases ($p = 0.002$ vs. controls) in mean PASP both during hypoxia (from 28+/-4 to 57+/-10 mm Hg, deltaPASP 28.7+/-6 mm Hg) and during exercise (from 28+/-4 to 55+/-11 mm Hg, deltaPASP 27+/-8 mm Hg) than did control subjects. Stress echocardiography allowed discrimination between groups without overlap using a cut off PASP value of 45 mm Hg at work rates less than 150 W. CONCLUSIONS: These data indicate that HAPE-S subjects may have abnormal pulmonary vascular responses not only to hypoxia but also to supine bicycle exercise under normoxic conditions. Thus, Doppler echocardiography during supine bicycle exercise or after 90 min of hypoxia may be useful noninvasive screening methods to identify subjects susceptible to HAPE.

Publication Types:
- Clinical Trial

MeSH Terms:

- Adult
- Altitude Sickness/physiopathology
- Altitude Sickness/ultrasonography*
- Anoxia/physiopathology
- Anoxia/ultrasonography
- Blood Gas Analysis
- Echocardiography, Doppler*
- Exercise Test*
- Human
- Male
- Middle Age
- Mountaineering
- Prospective Studies
- Pulmonary Edema/physiopathology
- Pulmonary Edema/ultrasonography*
- Pulmonary Wedge Pressure/physiology
- Risk Factors
- Single-Blind Method
- Support, Non-U.S. Gov't
- Systole/physiology
- Ventricular Function, Left/physiology

PMID: 10732898 [PubMed - indexed for MEDLINE]

1: Cytokine. 2000 Mar;12(3):246-52.

ELSEVIER SCIENCE FULL-TEXT ARTICLE

High altitude increases circulating interleukin-6, interleukin-1 receptor antagonist and C-reactive protein.

Hartmann G, Tschop M, Fischer R, Bidlingmaier C, Riepl R, Tschop K, Hautmann H, Endres S, Toepfer M.

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Hypoxic pulmonary vasoconstriction is associated with but may not be sufficient for the development of high-altitude pulmonary oedema (HAPO). Hypoxia is known to induce an inflammatory response in immune cells and endothelial cells. It has been speculated that hypoxia-induced inflammatory cytokines at high altitude may contribute to the development of HAPO by causing capillary leakage in the lung. We were interested if such an inflammatory response, possibly involved in a later development of HAPO, is detectable at high altitude in individuals without HAPO. We examined the plasma levels of interleukin 6 (IL-6), interleukin 1 receptor antagonist (IL-1ra) and C-reactive protein (CRP) in two independent studies: study A, Jungfraujoch, Switzerland, three overnight stays at 3458 m, n=12; study B: Capanna Regina Margherita, Italy, 3 overnight stays at 3647 m and one overnight stay at 4559 m, n=10. In both studies, probands showed symptoms of acute mountain sickness but no signs of HAPO. At the Jungfraujoch, IL-6 increased from 0.1+/-0.03 pg/ml to 2. 0+/-0.5 pg/ml (day 2, P=0.03), IL-1ra from 101+/-21 to 284+/-73 pg/ml (day 2, P=0.01), and CRP from 1.0+/-0.4 to 5.8+/-1.5 micrograms/ml (day 4, P=0.01). At the Capanna Margherita, IL-6 increased from 0. 5+/-0.2 pg/ml to 2.0+/-0.8 pg/ml (P=0.02), IL-1ra from 118+/-25 to 213+/-28 pg/ml (P=0.02), and CRP from 0.4+/-0.03 to 3.5+/-1.1 micrograms/ml (P=0.03). IL-8 was below the detection limit of the ELISA (<25 pg/ml) in both studies. The increase of IL-6 and IL-1ra in response to high altitude was delayed and preceded the increase of CRP. We conclude that: (1) circulating IL-6, IL-1ra and CRP are upregulated in response to hypobaric hypoxic conditions at high altitude, and (2) the moderate systemic increase of these inflammatory markers may reflect considerable local inflammation. The existence and the kinetics of high altitude-induced cytokines found in this study support the hypothesis that inflammation is involved in the development of HAPO. Copyright 2000 Academic Press.

MeSH Terms:

- Adult
- Altitude
- Altitude Sickness/blood*
- Altitude Sickness/metabolism
- C-Reactive Protein/metabolism*
- Female
- Human
- Inflammation/etiology
- Interleukin-6/blood*
- Male
- Oxygen/metabolism*
- Pulmonary Edema/blood*
- Pulmonary Edema/metabolism
- Receptors, Interleukin-1/antagonists & inhibitors*
- Receptors, Interleukin-1/metabolism
- Sialoglycoproteins/biosynthesis*
- Support, Non-U.S. Gov't

Substances:

- Interleukin-6
- Receptors, Interleukin-1
- Sialoglycoproteins
- interleukin 1 receptor antagonist protein
- Oxygen
- C-Reactive Protein

PMID: 10704252 [PubMed - indexed for MEDLINE]

1: Mayo Clin Proc. 1998 Oct;73(10):988-92; quiz 992-3. Related Articles, Links

Altitude-related illnesses.

Klocke DL, Decker WW, Stepanek J.

Division of Emergency Medical Services, Mayo Clinic Rochester, MN 55905, USA.

Altitude-related illnesses are a frequent cause of morbidity and occasional mortality in travelers to high altitudes in the United States and throughout the world. The primary altitude illnesses are acute mountain sickness, high-altitude pulmonary edema, and high-altitude cerebral edema. The pathogenesis of these syndromes remains unclear despite considerable research. Altitude also has potential deleterious effects on common medical conditions including coronary artery disease, pulmonary disease, hemoglobinopathies, and pregnancy. Most of these problems are primarily preventable with appropriate information before travel. Education should include information about rate of ascent, diet, alcohol intake, physical activity, and preventive medications, including acetazolamide, nifedipine, and dexamethasone in selected circumstances.

Publication Types:
- Review
- Review, Tutorial

MeSH Terms:
- Altitude Sickness*/complications
- Altitude Sickness*/physiopathology
- Altitude Sickness*/prevention & control
- Altitude Sickness*/therapy
- Brain Edema/etiology
- Cerebrovascular Circulation
- Chronic Disease
- Female
- Human
- Pregnancy
- Pregnancy Complications
- Pulmonary Edema/etiology

PMID: 9787751 [PubMed - indexed for MEDLINE]

☐ 1: Crit Care Clin. 1999 Apr;15(2):265-80, viii.

Related Articles, Links

Altitude-related pulmonary disorders.

Krieger BP, de la Hoz RE.

Division of Pulmonary and Critical Care, University of Miami at Mount Sinai Medical Center, Florida, USA.

The major physiologic stress encountered at high altitude is caused by the occurrence of hypobaric hypoxia. In this article, acute and chronic pulmonocardiac adaptation to altitude is reviewed, including possible genetic differences among highlanders from the Himalayan versus the Andean Mountains. The origin, symptoms, and treatment of acute mountain sickness and high altitude pulmonary edema are outlined. In addition, the prediction and prevention of pulmonary complications that may be encountered or exacerbated during commercial airflight are noticed.

Publication Types:
- Review
- Review, Tutorial

MeSH Terms:
- Altitude*
- Altitude Sickness/physiopathology
- Animal
- Human
- Lung Diseases/etiology*
- Lung Diseases/physiopathology
- Lung Diseases/therapy
- Pulmonary Edema/etiology
- Pulmonary Edema/physiopathology
- Respiration
- Sleep Disorders/etiology

PMID: 10331128 [PubMed - indexed for MEDLINE]

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